Putting the pieces together again: genes, child maltreatment and psychoanalysis

The 33rd Annual Daniel S. Prager Lecture

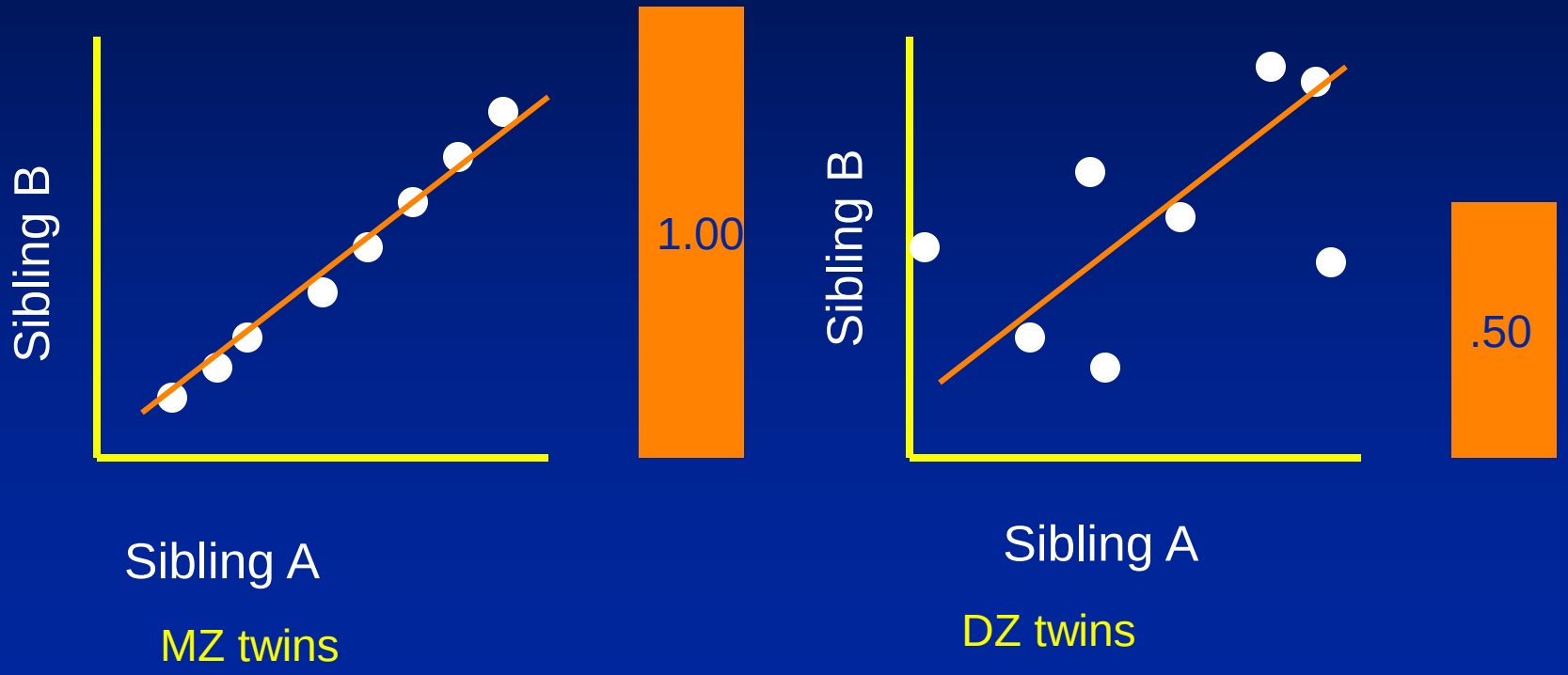
David Reiss, MD

Yale Child Study Center

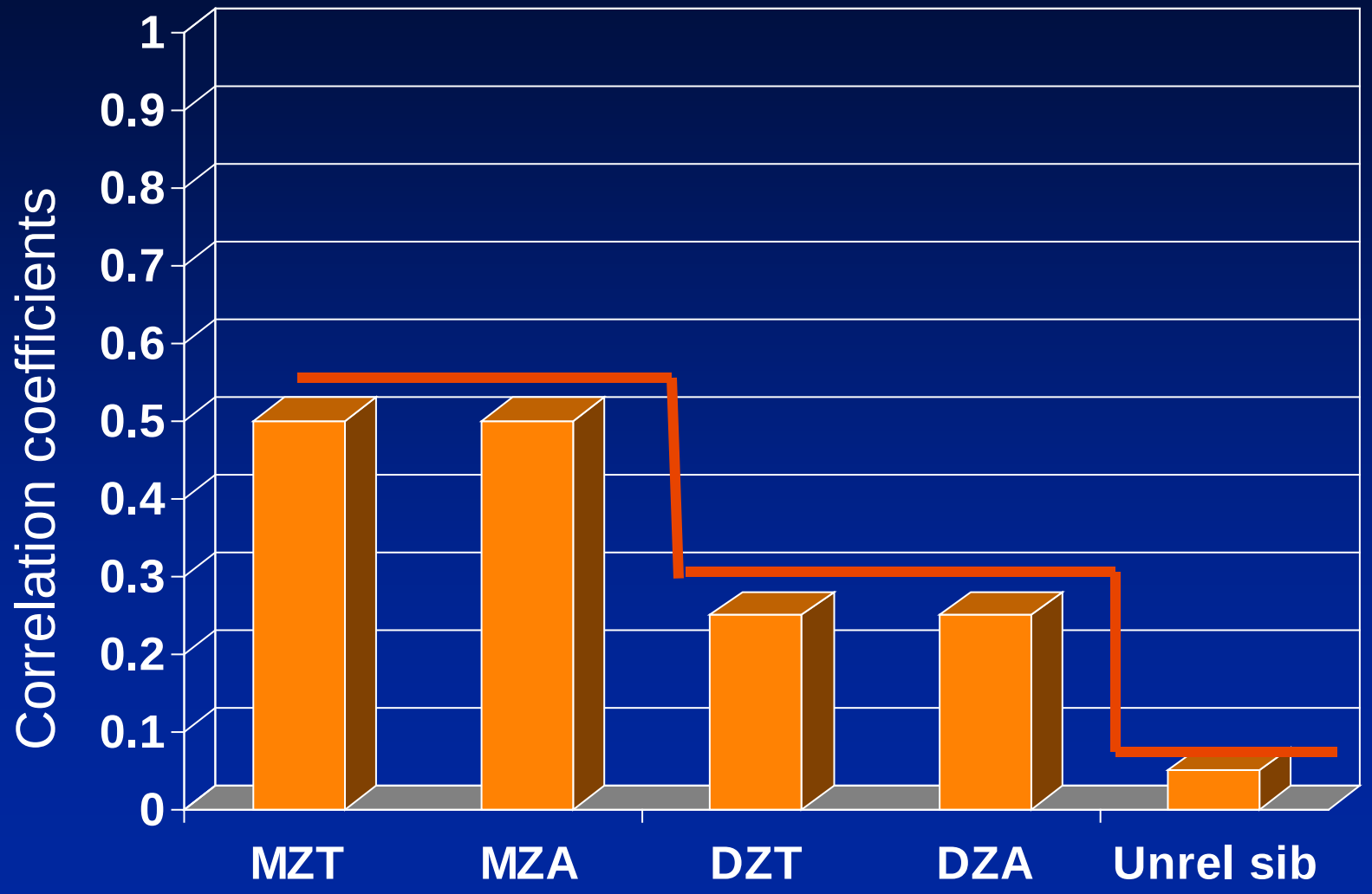
May 1, 2014

Robert Plomin

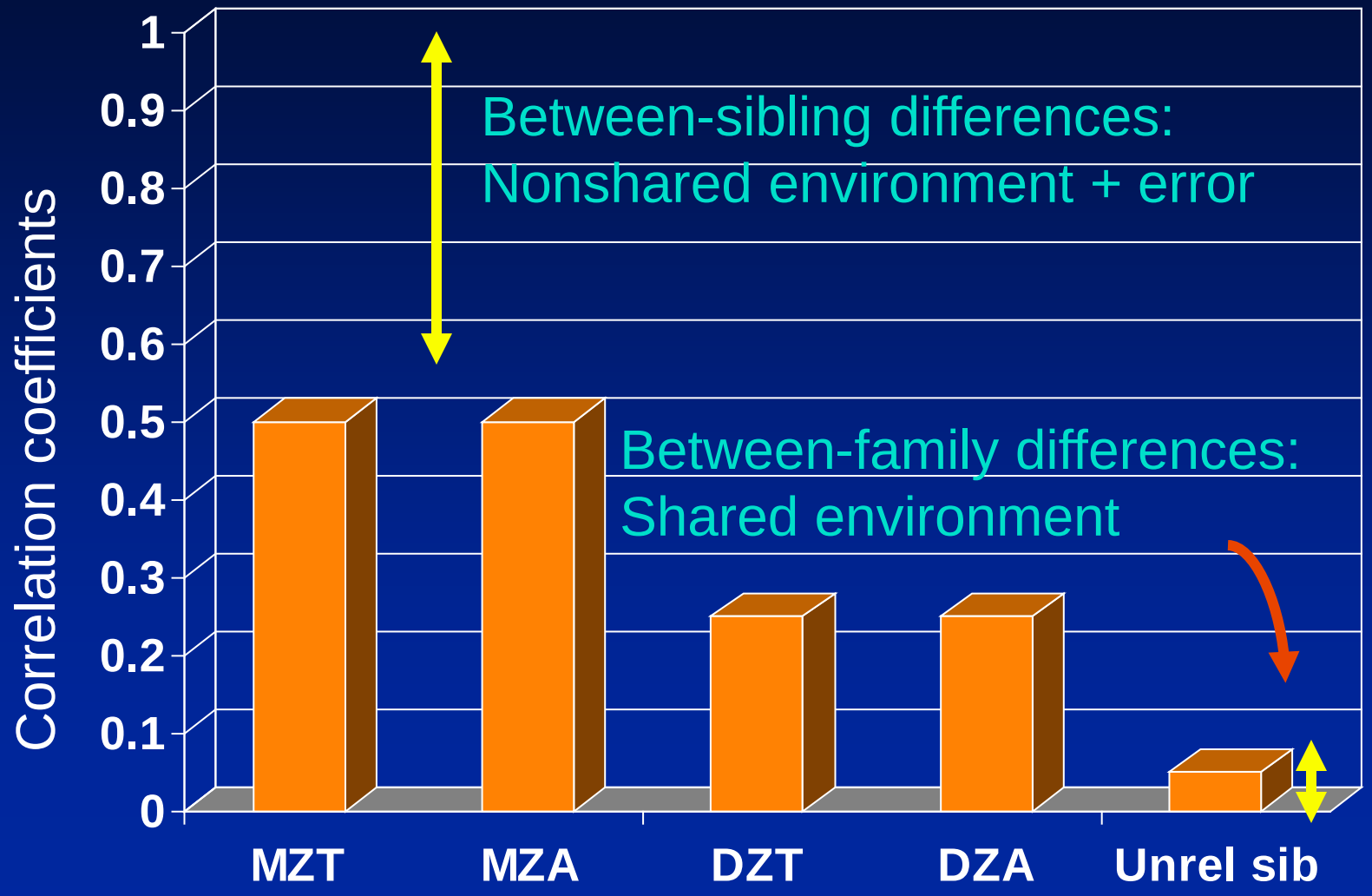
Comparison of MZ (identical) and DZ (fraternal) twins: comparing heights within twin pairs (contrived data)



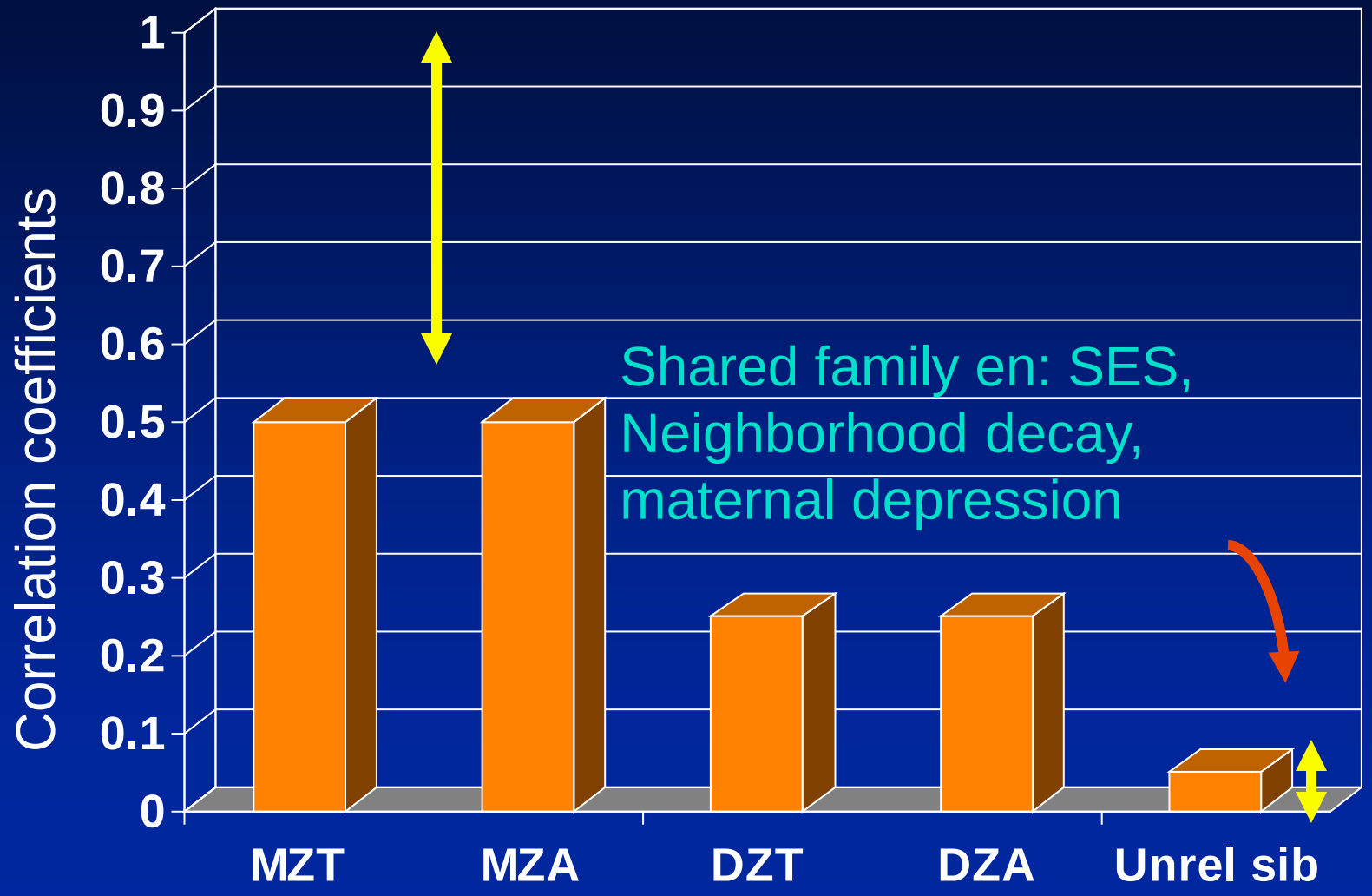
Summary of data from Plomin's studies Twins reared together (T) and Apart (A)
MZ= monozygotic DZ = dizygotic



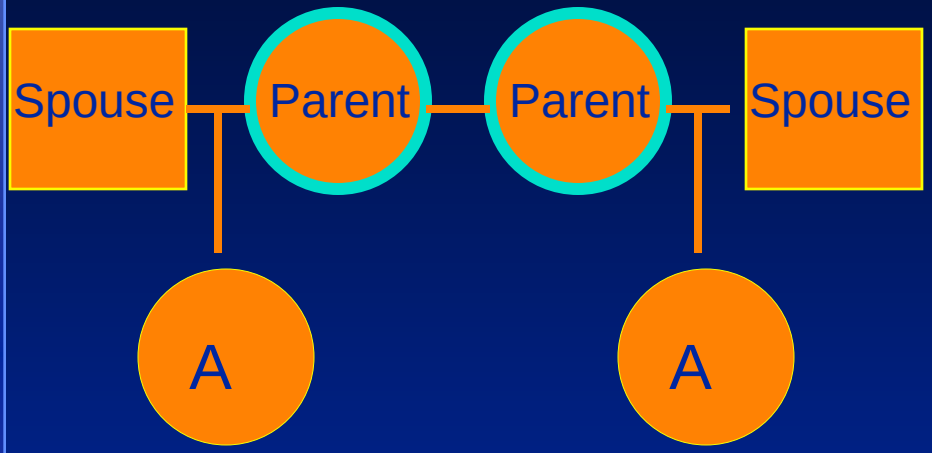
Summary of Plomin's data

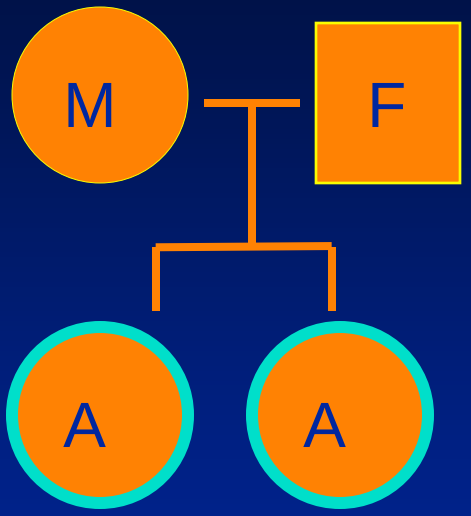


Summary of Plomin's data



MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)

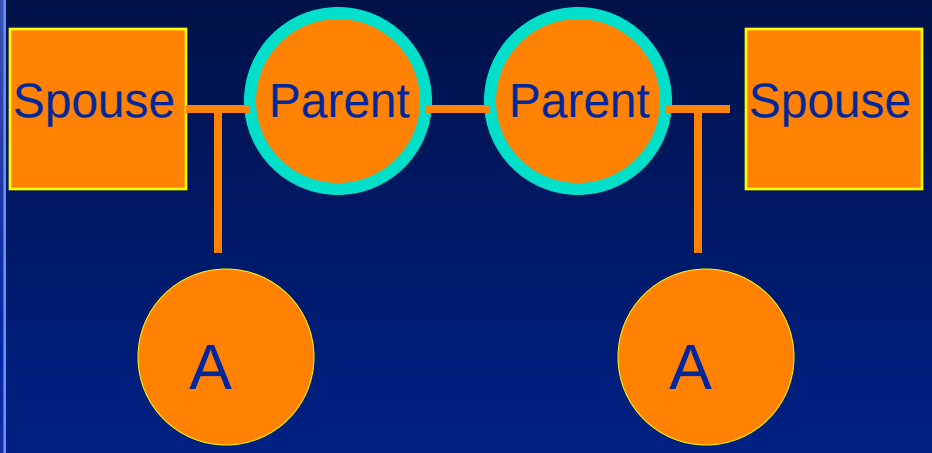


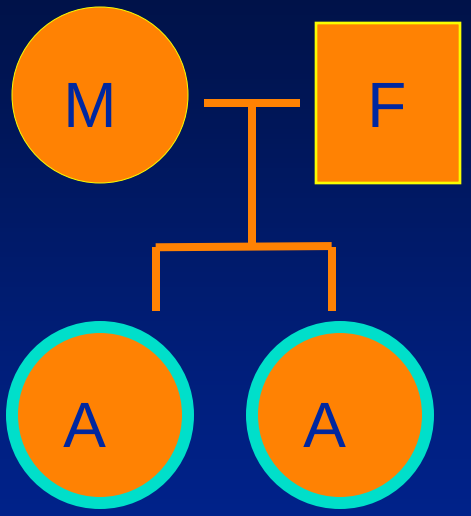


Sib type (P -P)		Genetic relatedness
254	MZ moms	100%
284	DZ moms	50%
128	MZ dads	100%
183	DZ dads	50%

Sib type (A-A)		Genetic relatedness
93	MZ	100%
99	DZ	50%
95	FS-non div	50%
182	FS-step	50%
109	HS-step	25%
130	Blended step	0%

MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)





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Adolescent antisocial behavior

OBSERVER CODE

PARENT AND CHILD REPORT

Disruptive, rude, aggressive, coercive behavior

school behavior

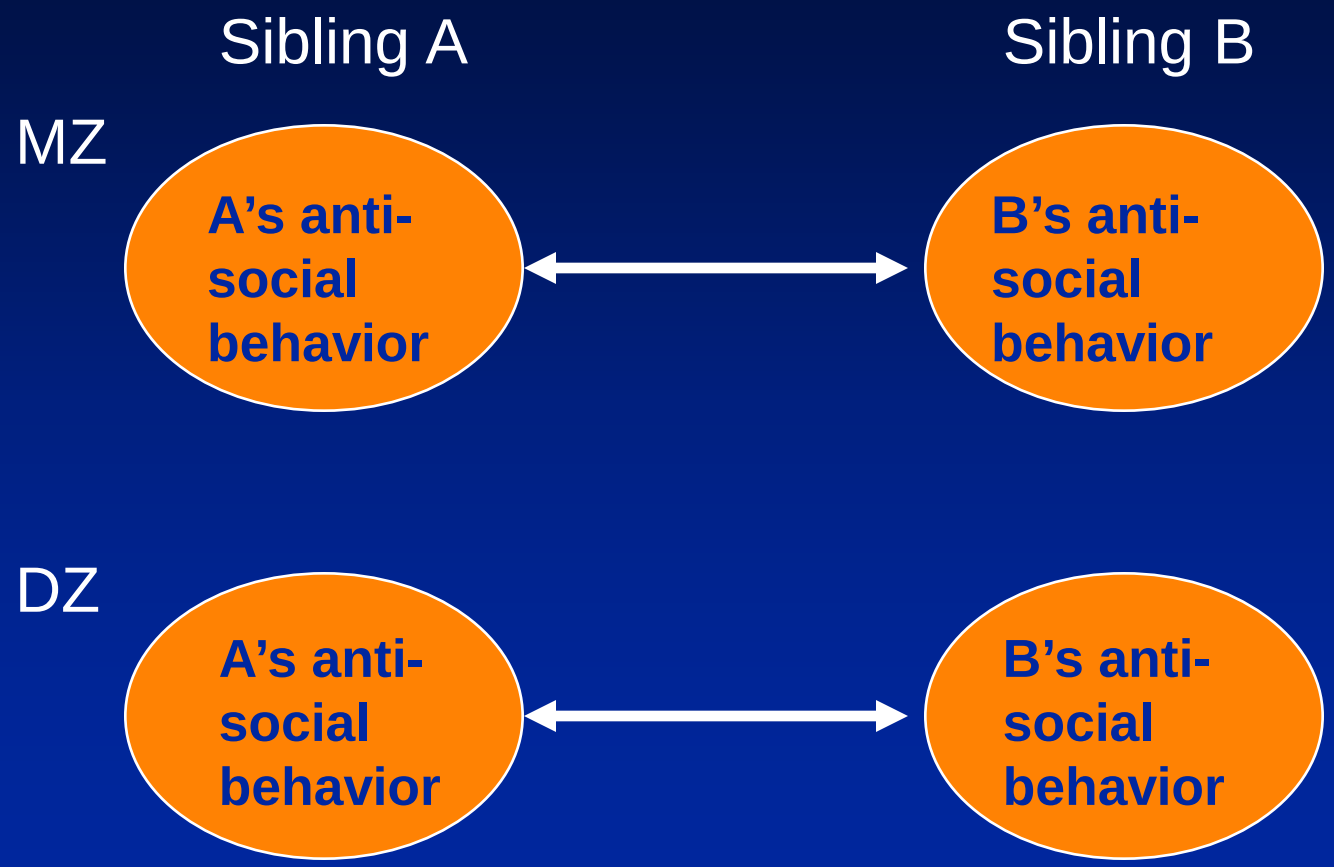
Trouble in school, skipped school mean, bully.

Stole, lied, cheated

brief, in home video

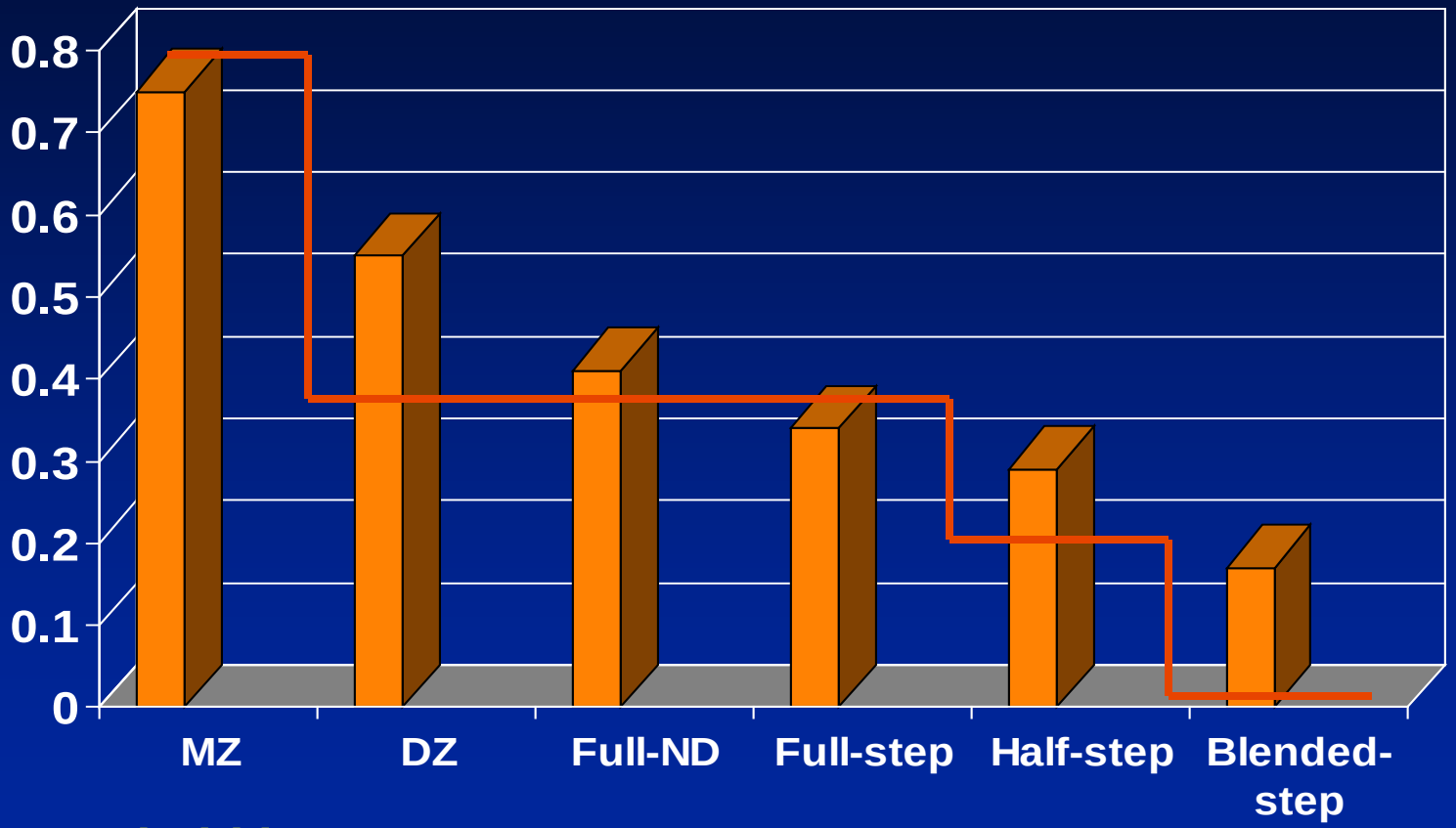
home and neighborhood

Illustration of within sib pair correlations for estimating genetic influence on antisocial behavior



Antisocial behavior: Mother, father, child and observer reports

Numbers on vertical axis are intraclass correlations within sibships



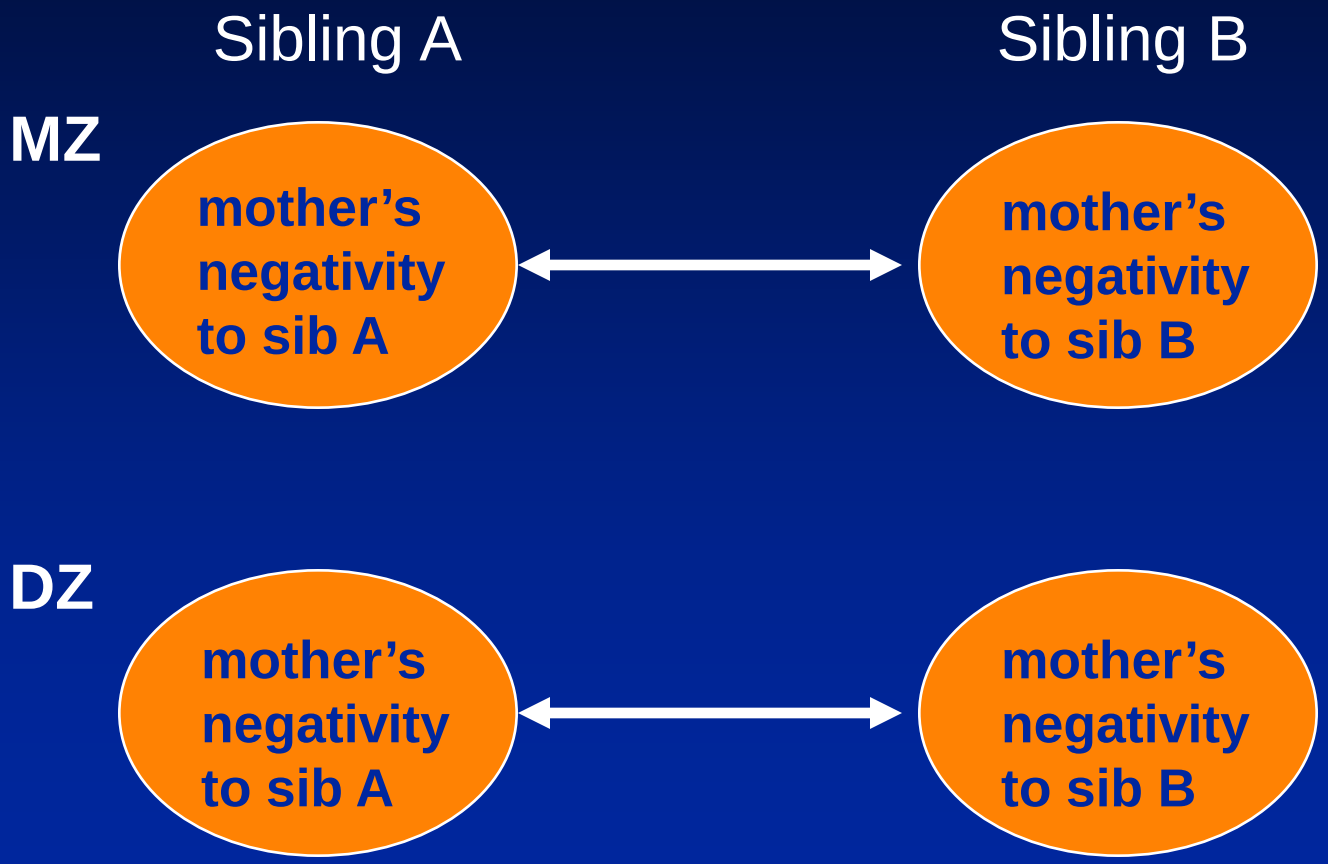
Heritability = 67%

Environmentality: Shared = 12% Nonshared = 21%

Parent-child negativity:

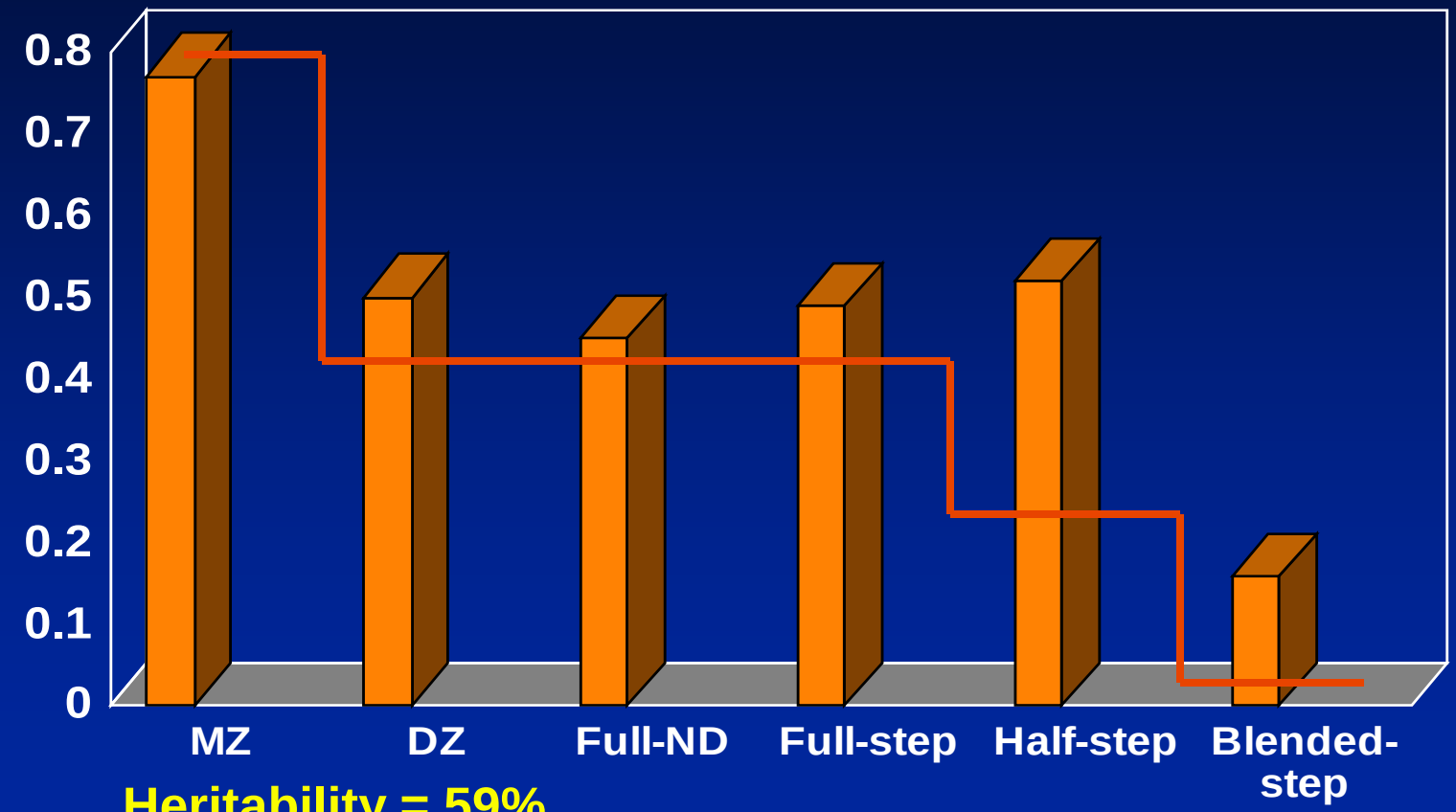
OBSERVER CODES	PARENT AND CHILD REPORT
Anger and rejection	Disagreement
Coercion	Punitiveness
Conflict	Yielding to coercion
	Open conflict
	Verbal aggression

Illustration of within sibling correlations for detecting genetic influences on mother's negativity



Mother's negativity towards child: within sibship correlations across sibling types.

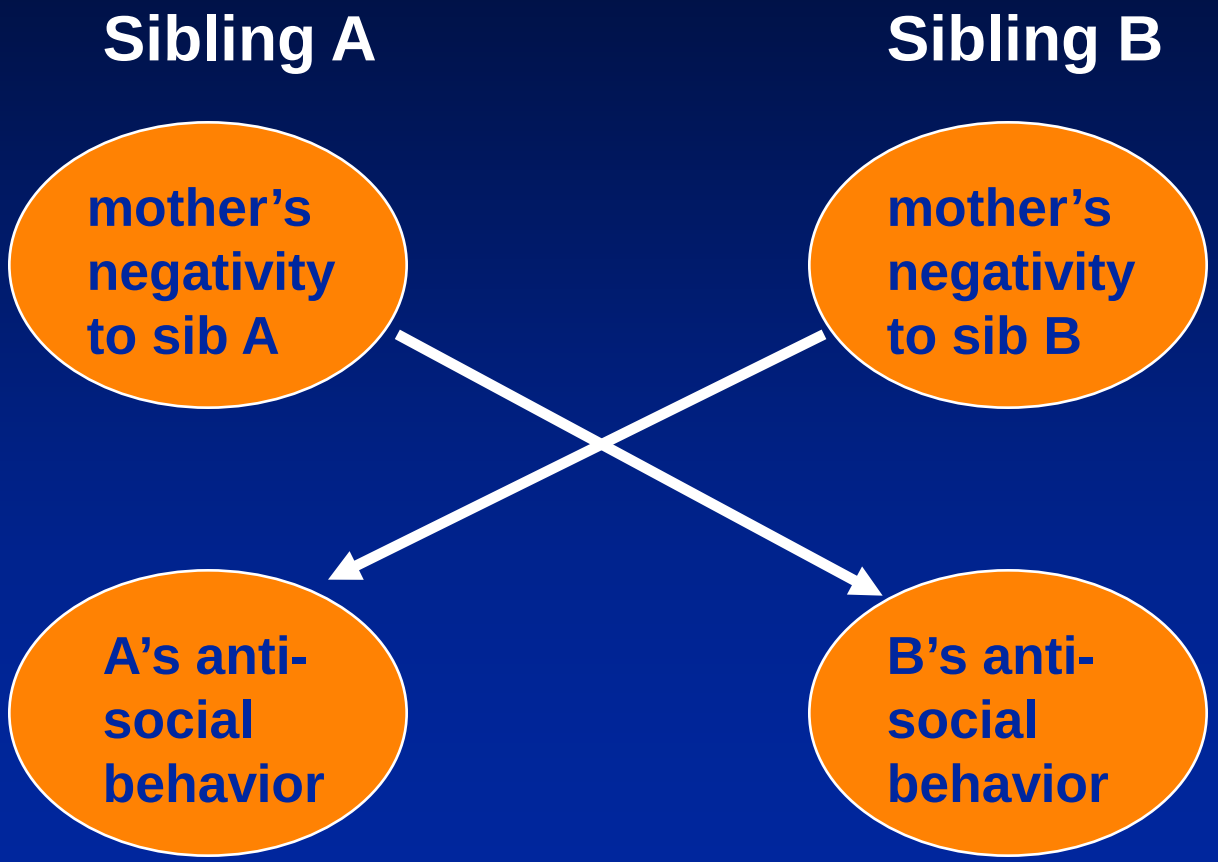
Numbers on vertical axis are intraclass correlations within sibships



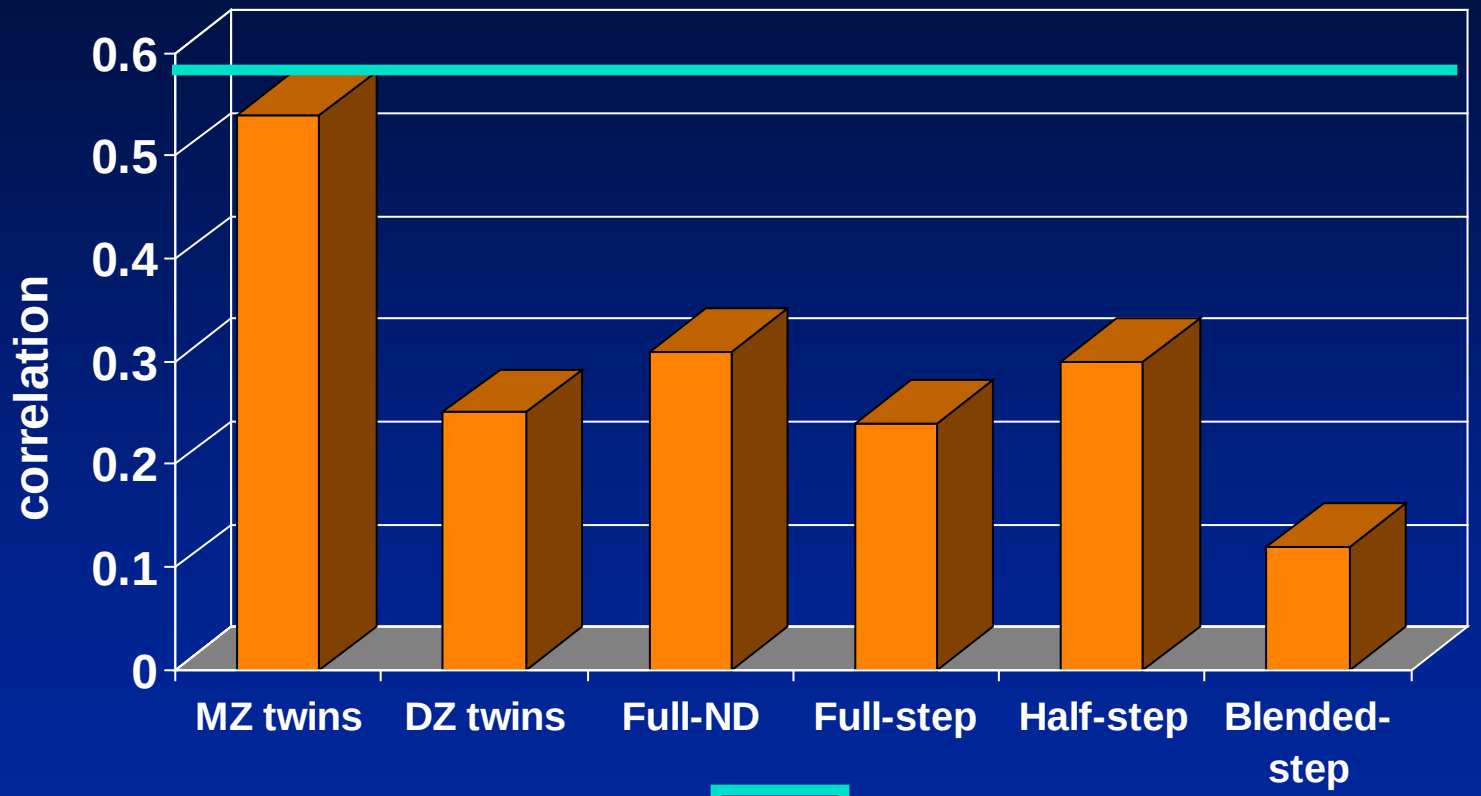
Heritability = 59%

Environmentality: Shared = 15% Nonshared = 26%

Illustration of *cross-variable*, within-sib pair correlations for detecting overlap of genetic influences



Overlapping genetic influences on mother's negativity and adolescent antisocial behavior:
comparing *cross variable,* within sib pair correlations

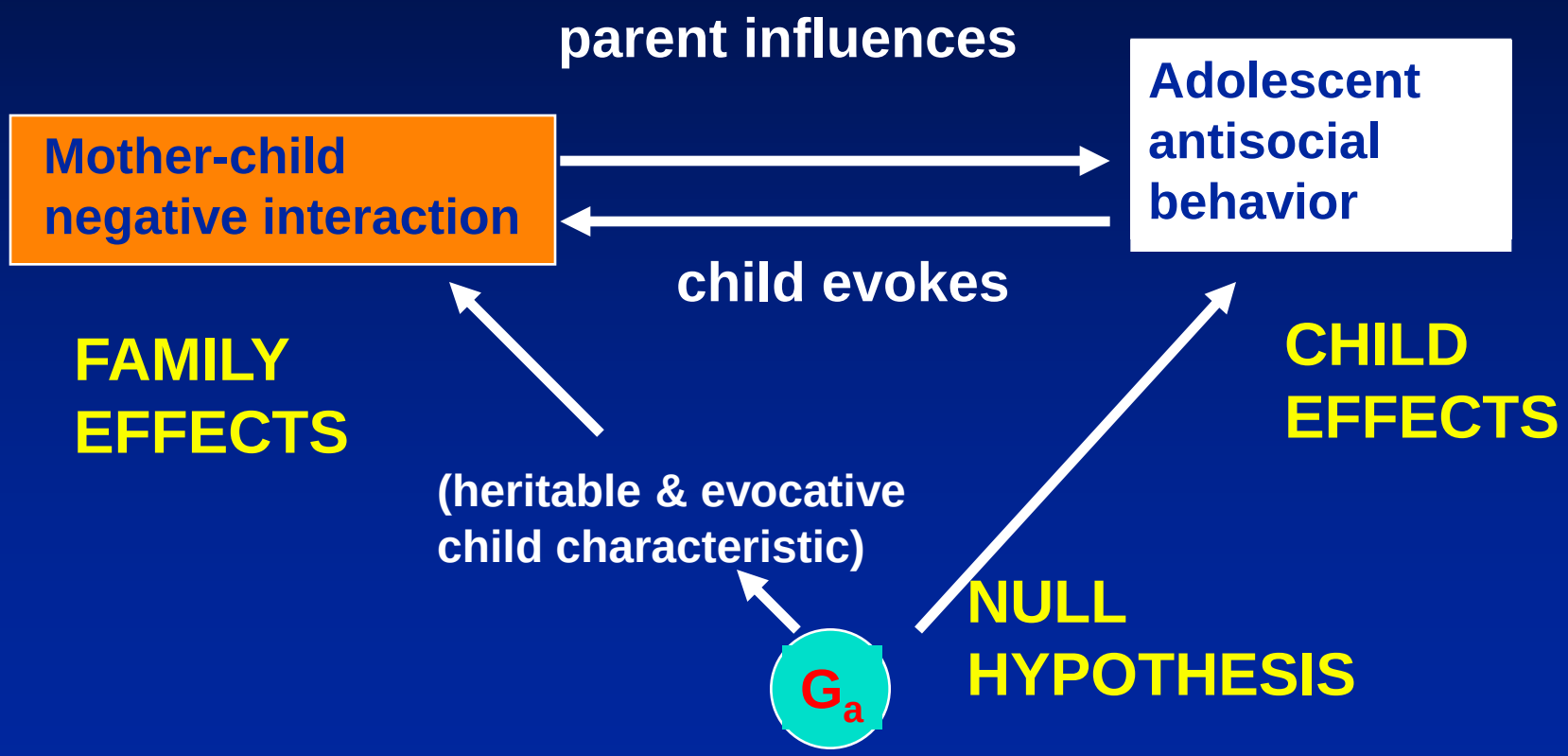


phenotypic correlation = .59

68% of this corr. is attributable to G

27% of this corr. is attributable to SE

Evocative gene-environment correlations: null hypothesis, family effects and child effects versions



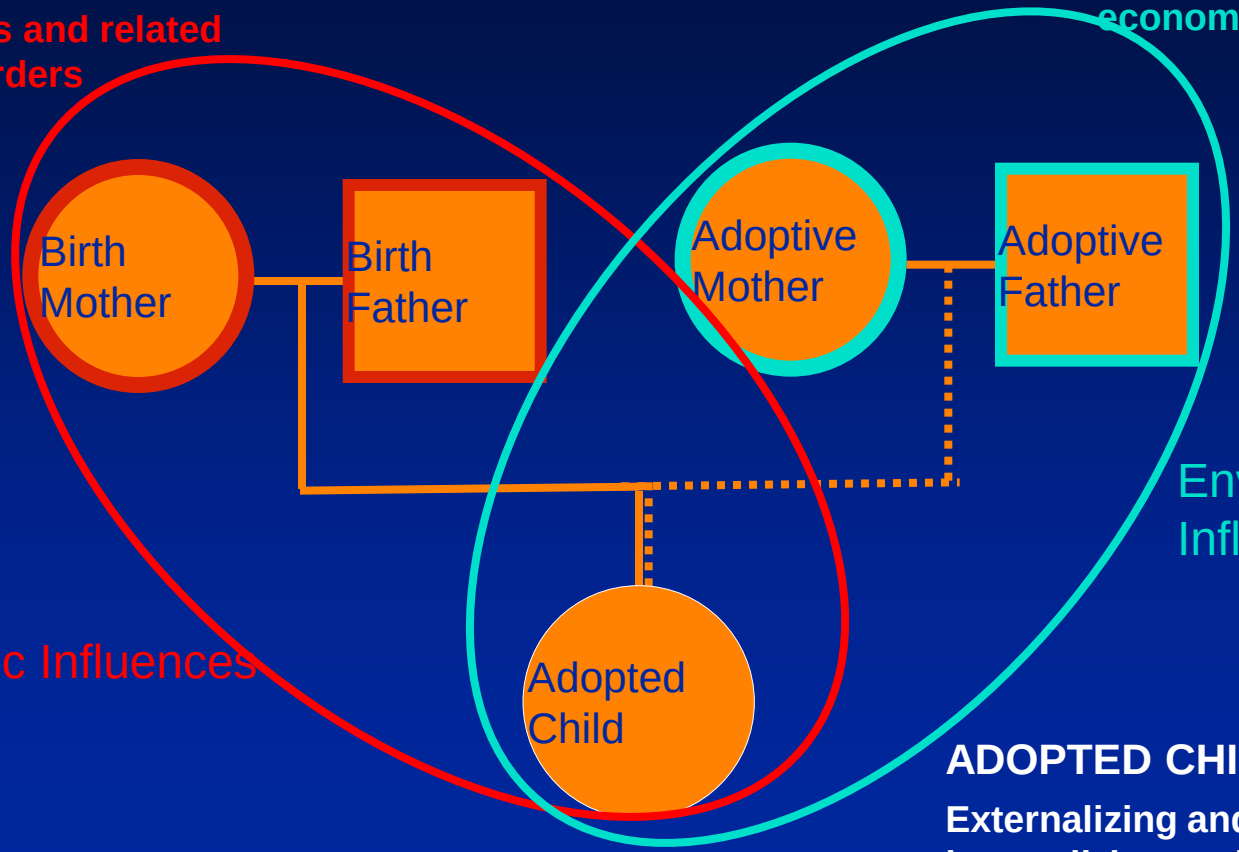
Early Growth & Development Study
n=361 expanded to n = 561

BIRTH PARENTS

SUDs and related disorders

ADOPTIVE PARENTS

Parenting in the context of depression, marital problems and economic worries



ADOPTED CHILDREN

Externalizing and internalizing problems

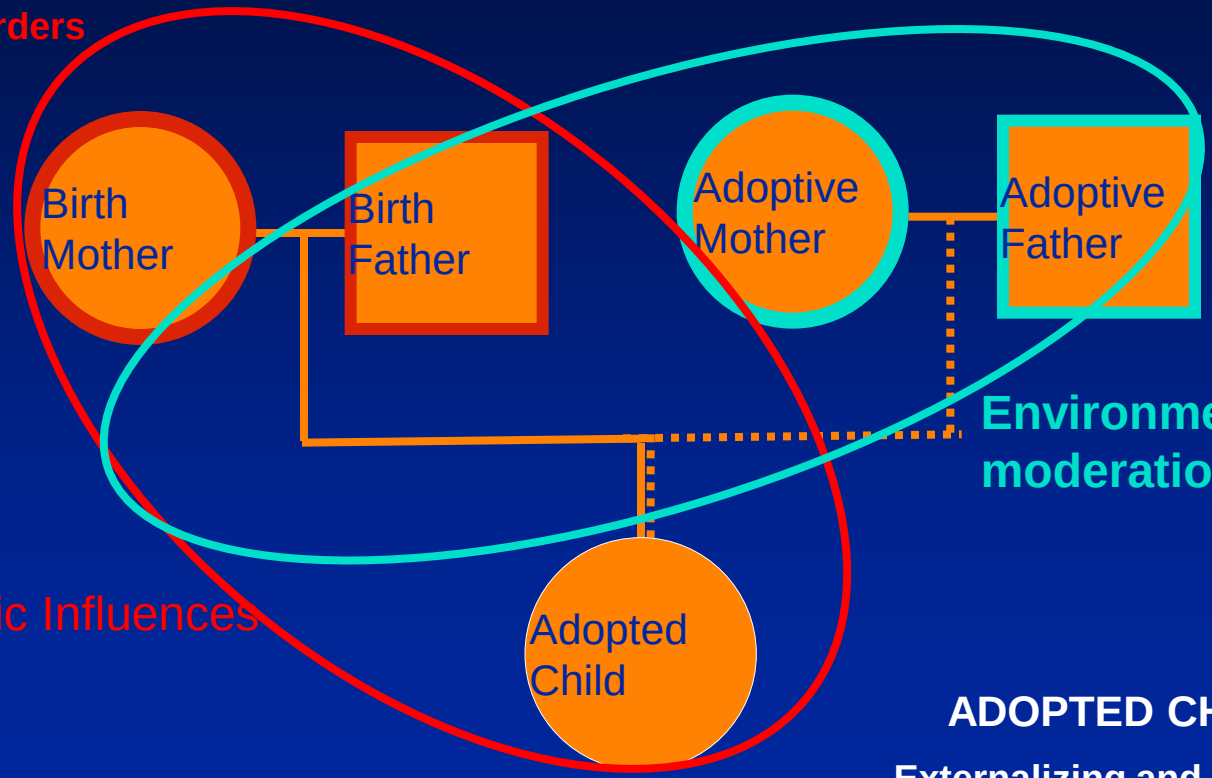
Early Growth & Development Study

ADOPTIVE PARENTS

Parenting in the context of depression, marital problems and economic worries

BIRTH PARENTS

SUDs and related disorders



ADOPTED CHILDREN

Externalizing and internalizing problems

Photo Source: Strategies for Success (Chandler, AZ), 2012

I can't understand my baby

I can't make my baby look at me

I don't know what games and toys my baby likes

My kid struggles over bed time

Baby sitters are hard to find

Always cleaning up messes of toys and food

When my child misbehave I raise my voice and yell

When I am under stress I am picky and on my child's back

Items slightly paraphrased from D. S. Arnold (1993), KA Crnic (1990) and DM Teti (1991)

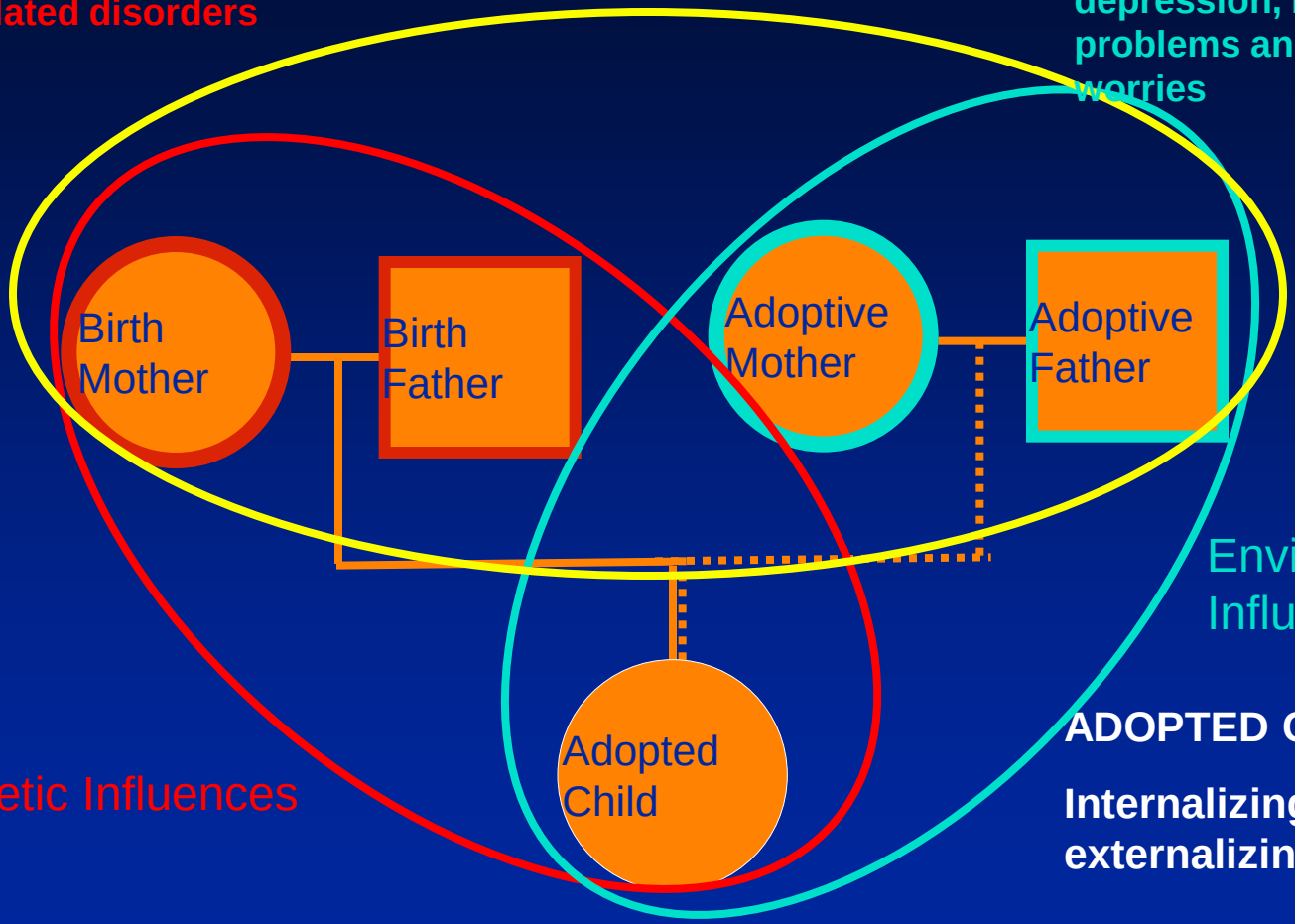
Early Growth & Development Study

Evocative influences

BIRTH PARENTS: SUDs and related disorders

ADOPTIVE PARENTS

Parenting in the context of depression, marital problems and economic worries



Environmental Influences

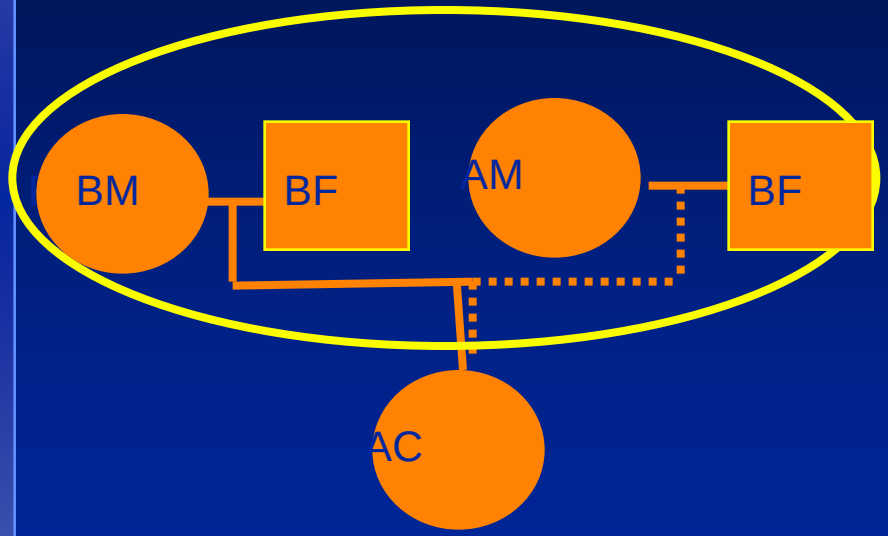
Genetic Influences

ADOPTED CHILDREN

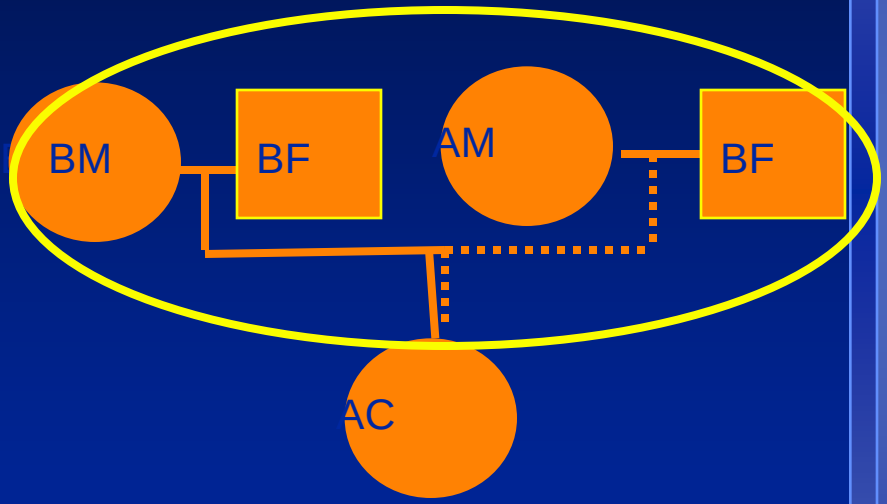
Internalizing and externalizing problems

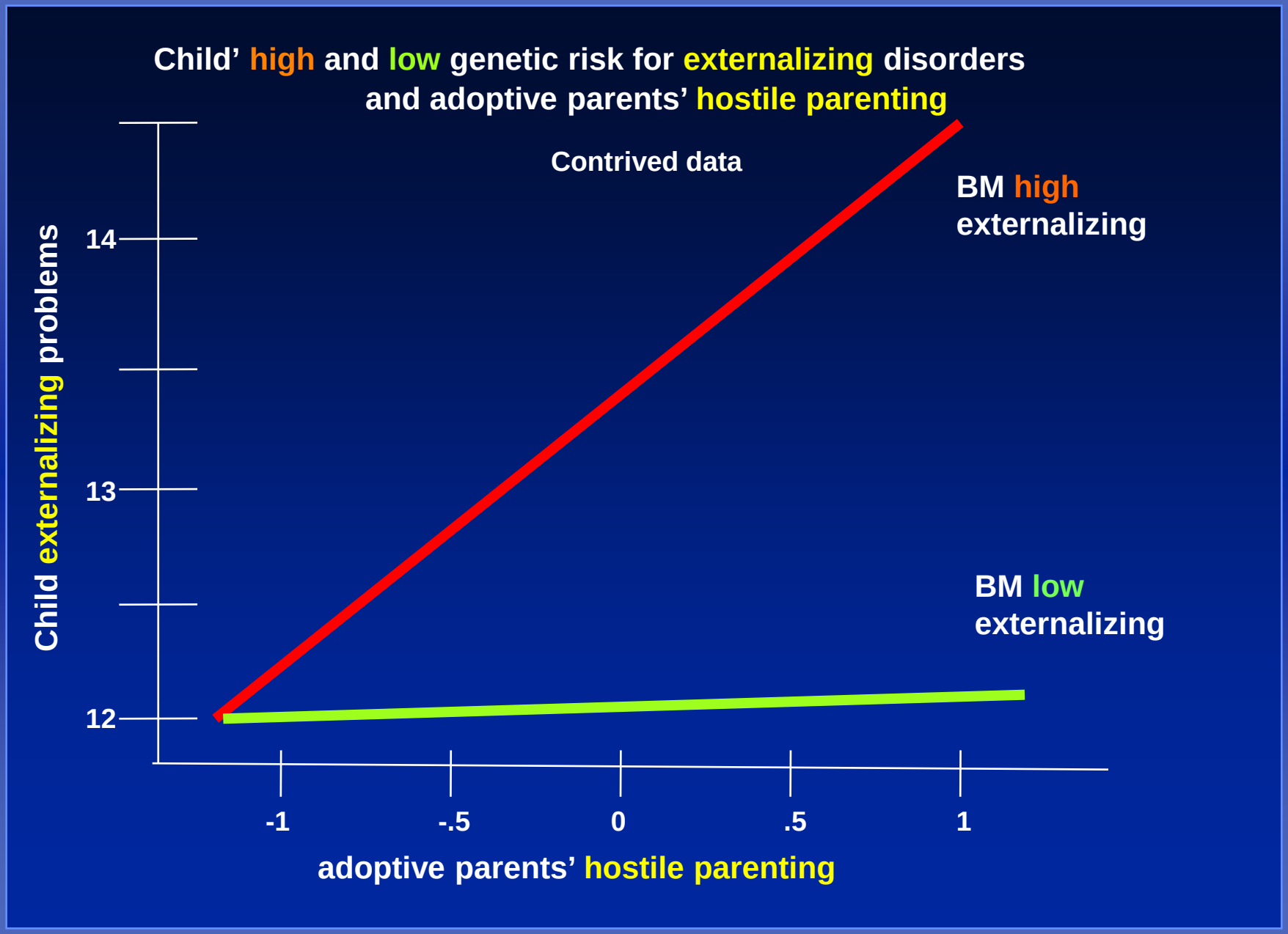
Prospective adoption study

Adoptive Parents in ADVERSE CONTEXT

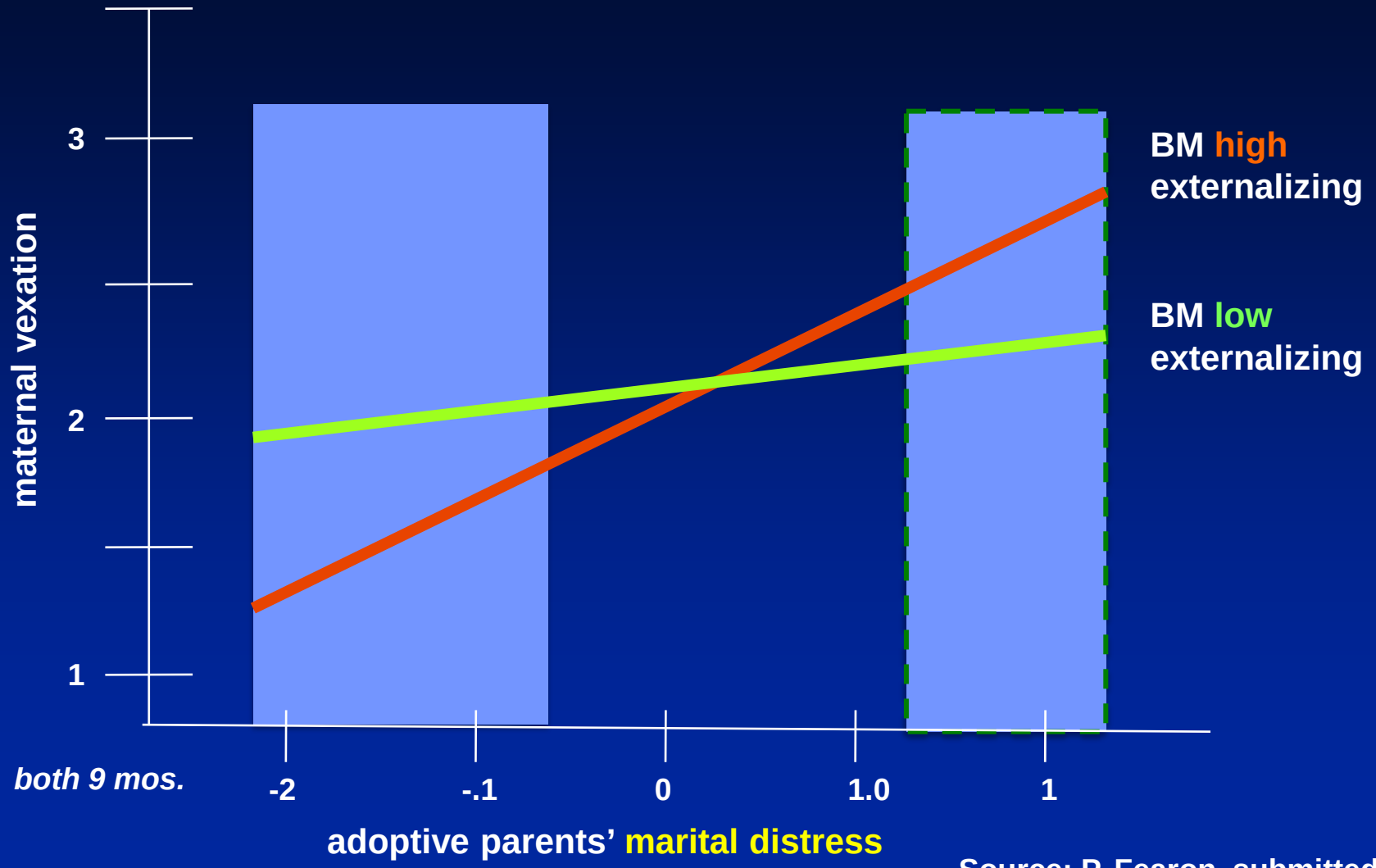


Adoptive Parents in FAVORABLE CONTEXT

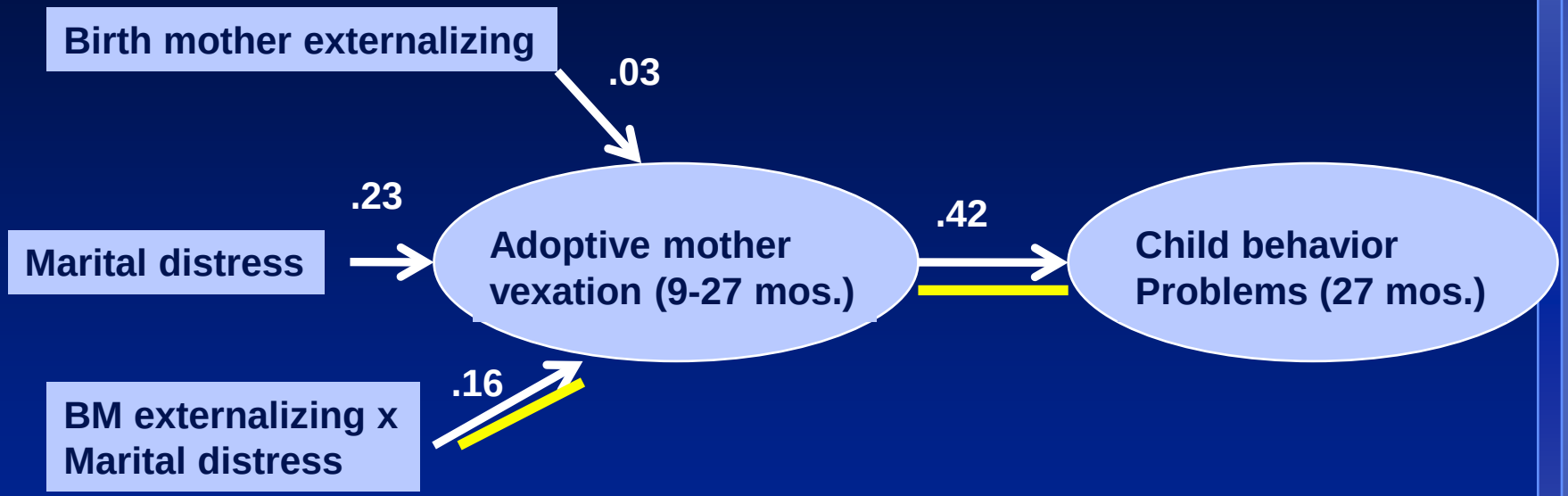


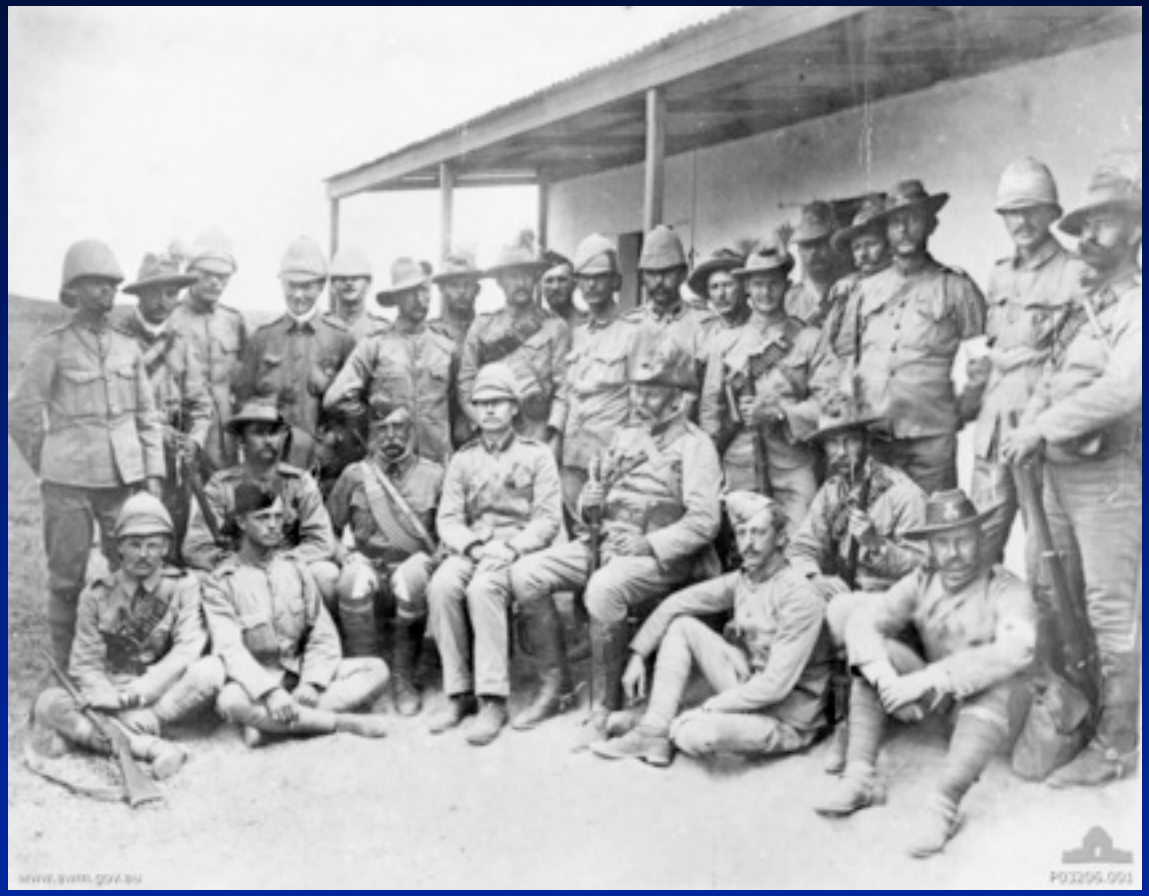

Child' high and low genetic risk for externalizing disorders
and adoptive parents' hostile parenting
Contrived data
BM high externalizing
BM low externalizing
Child externalizing problems
14
13
12
-1
-.5
0
.5
1
adoptive parents' hostile parenting

Children high and low genetic risk for externalizing disorders and adoptive parents' marital satisfaction (n = 561)



Source: P. Fearon, submitted


Birth mother externalizing
.03
.23
Marital distress
Adoptive mother vexation (9-27 mos.)
.42
Child behavior Problems (27 mos.)
.16
BM externalizing x Marital distress


www.awm.gov.au
P03256.001

David Barker 1938-2013

BMJ VOLUME 297 9 JULY 1988

Low birth weight and hypertension

In their study of 77 men aged 28 Professor Gerhard Gennser and colleagues found a relation between increased diastolic blood pressure and low

D J P BARKER
C OSMOND

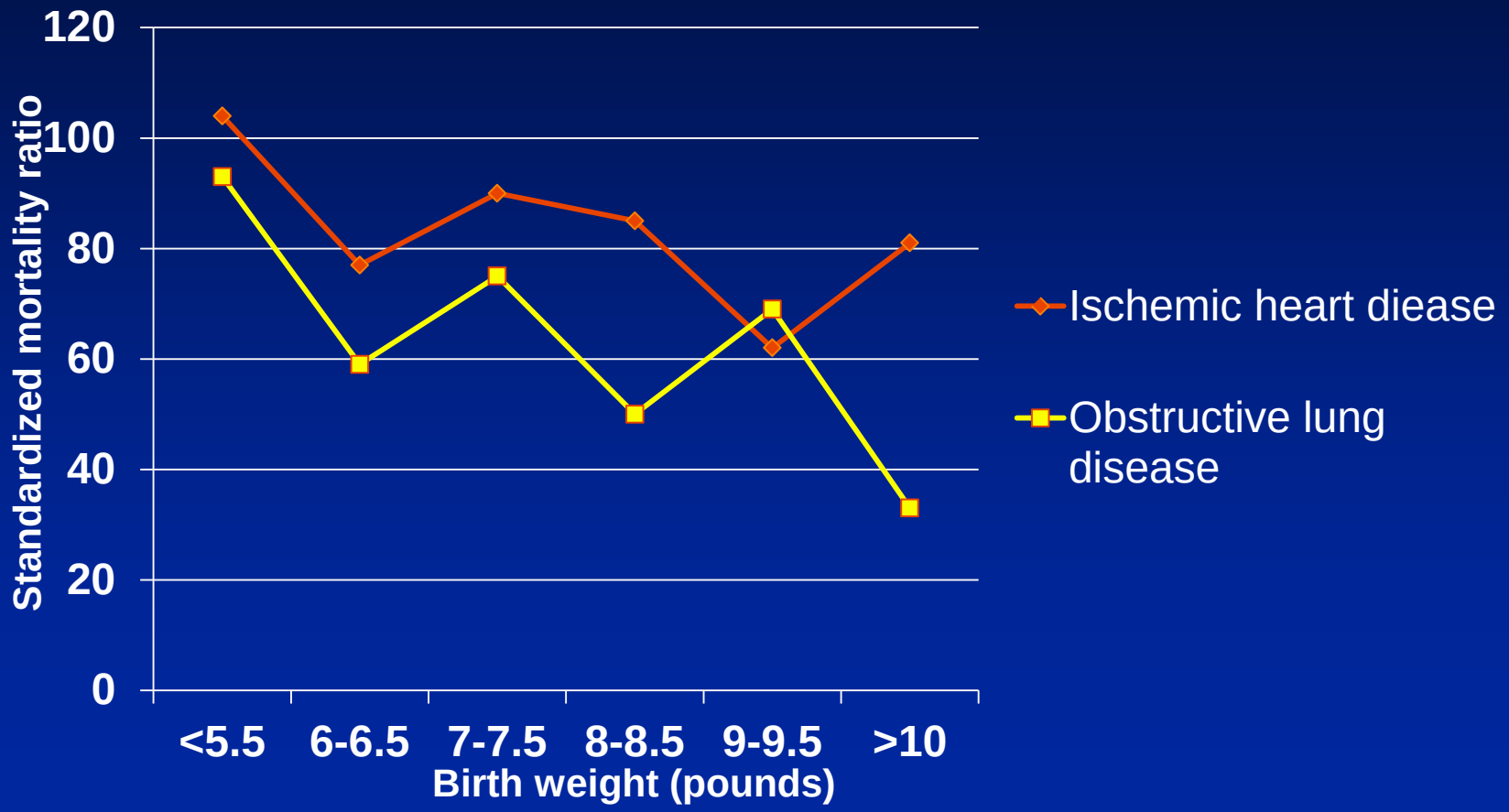
MRC Environmental Epidemiology Unit,
Southampton General Hospital,
Southampton SO9 4XY


SCOTLAND
Newcastle-upon-Tyne
Belfast
Barrow-in-Furness
Douglas
Liverpool
Holyhead
ENGLAND
WALES
Harwich
London
Tilbury
Tower Bridge
Greenwich
Milford Haven
Newport
Dover
Lundy Island
Southampton
Portsmouth
Plymouth
Portland
Fowey
Torquay
English Channel

Long term impact of restricted fetal growth: Standardized mortality ratios due to ischemic heat disease and chronic, obstructive pulmonary disease

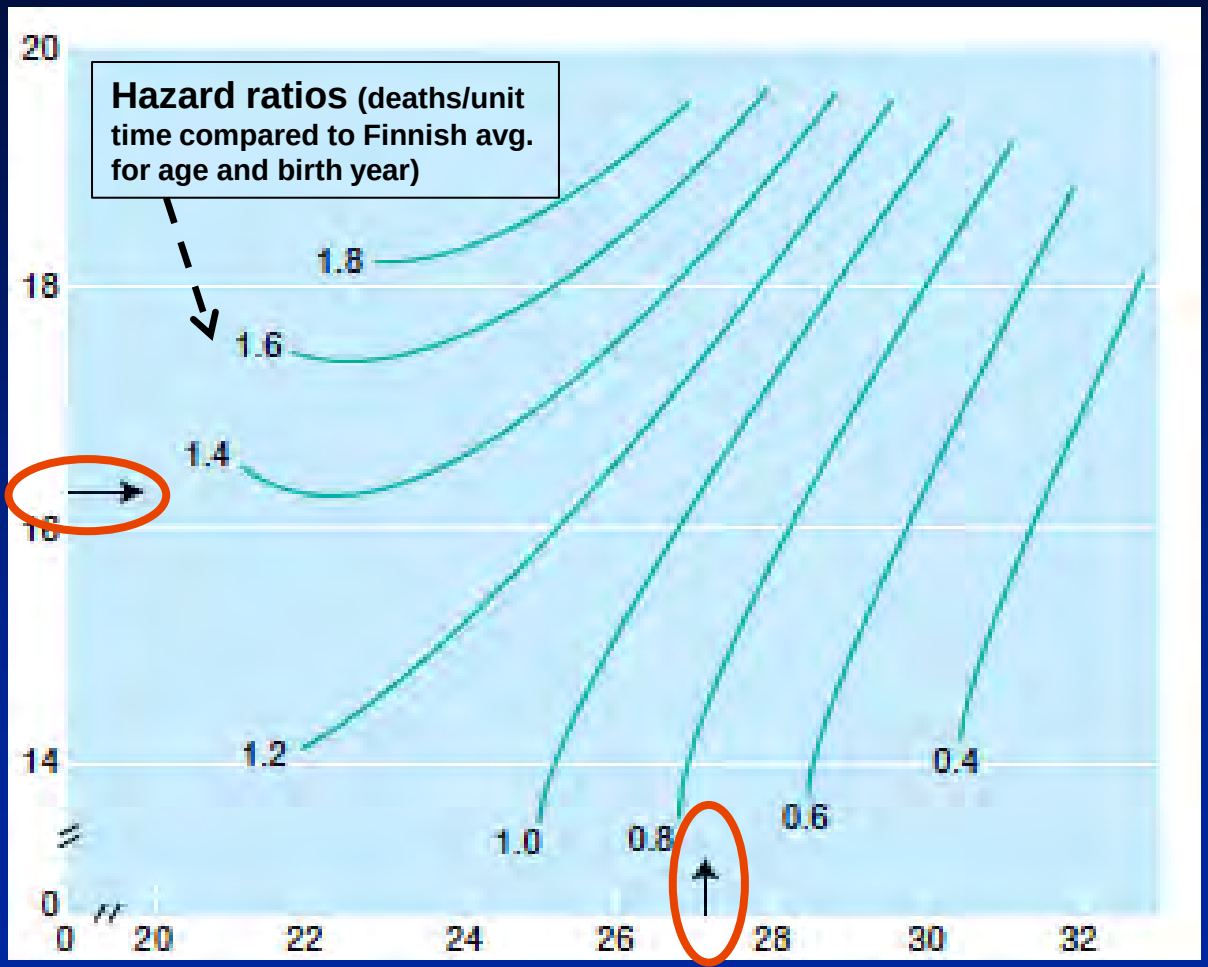
7991 men born in Hertfordshire between 1911-1930

source: DJP Barker et al 1989



Critical evidence for programming: the added risk of "catch-up" growth for *death from coronary artery disease*

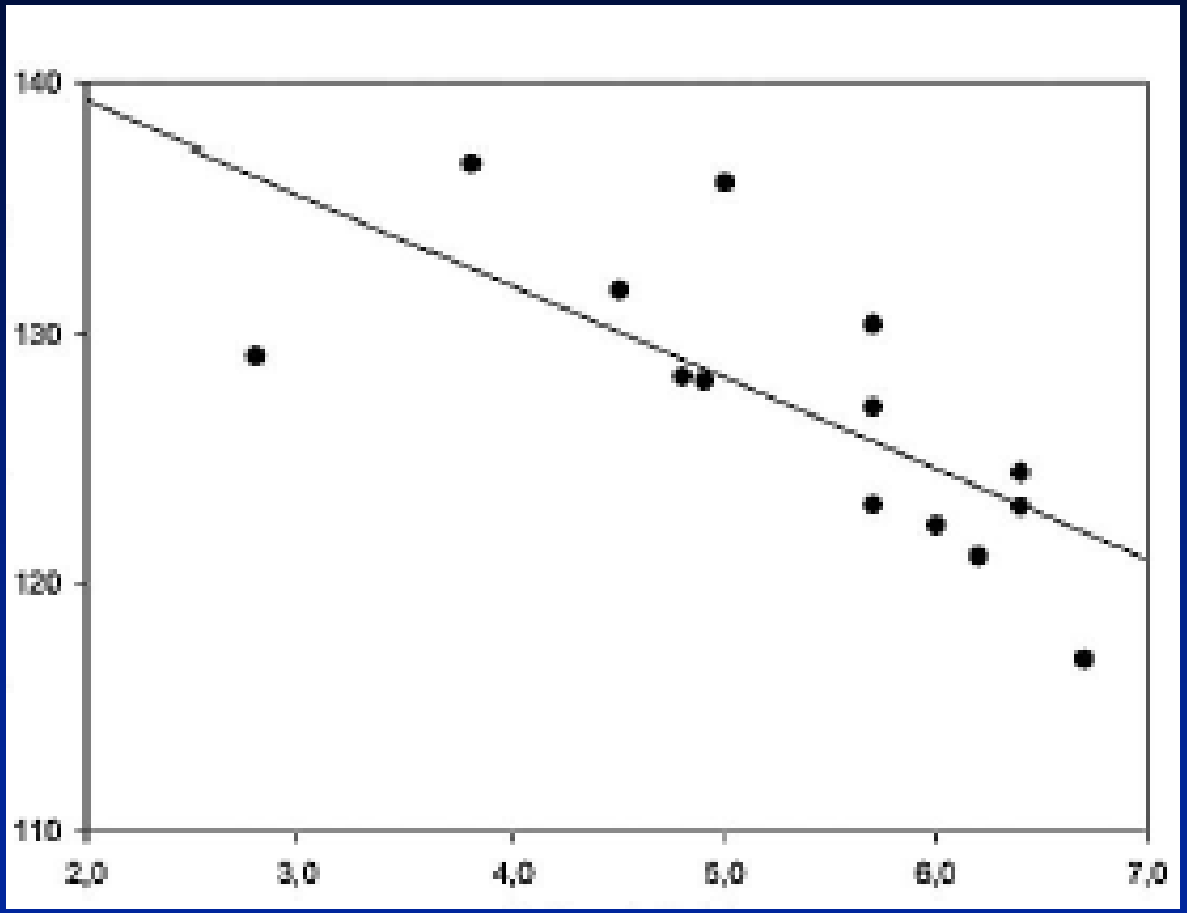
3641 men born in Helsinki between 1924 and 1933



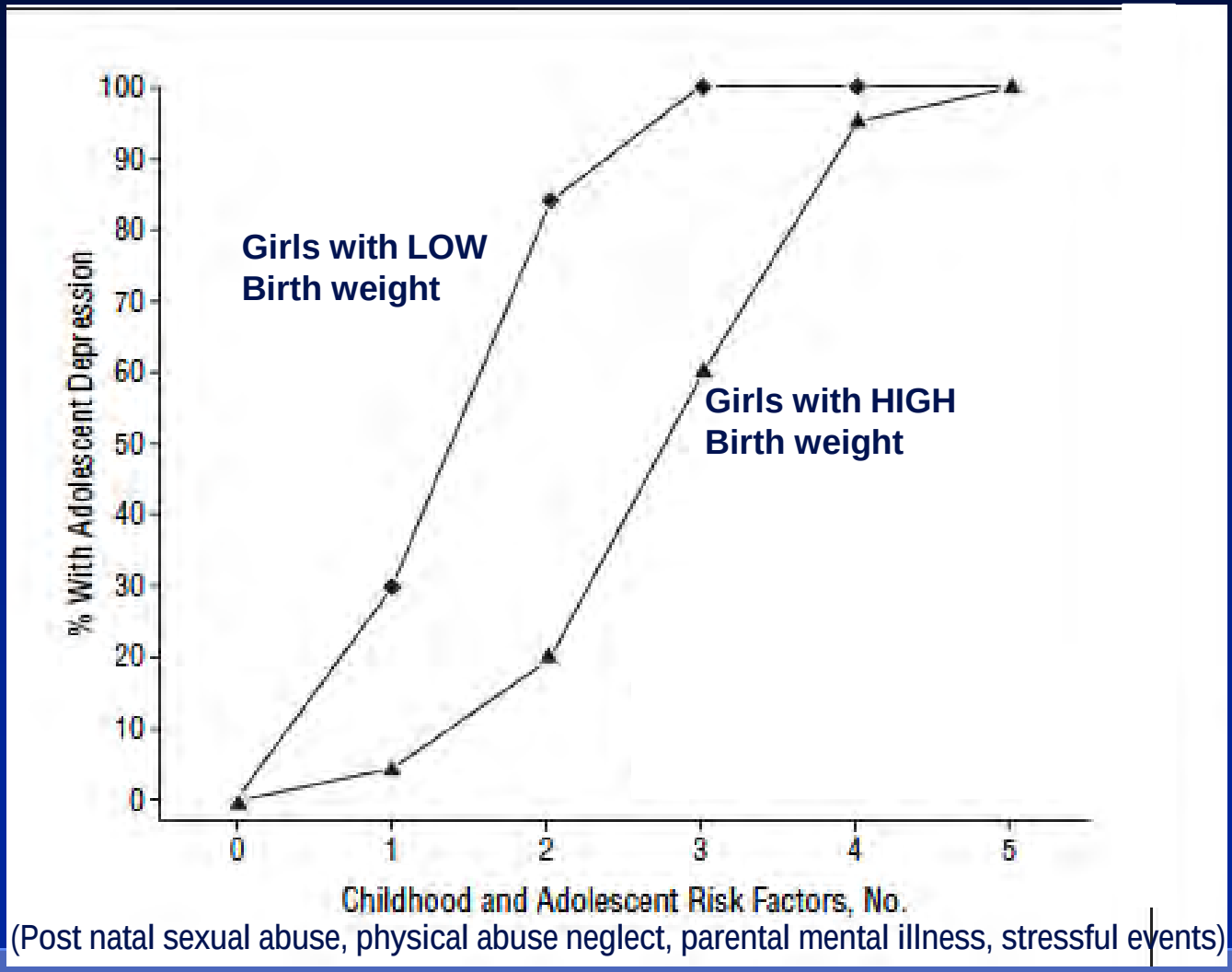
Source: JG Erikson, 1999

Confirmation of the effects of fetal growth restriction in a *rat model*: birth weight and adult (12 week) systolic BP

source : MF Shreuder et al, 2006



Low birth weight and depression in teenage girls (n= 1420)
n=81 low birth weight(< 5.5 lbs)
Source: Great Smoky Mountain Study EJ Costello, 2007

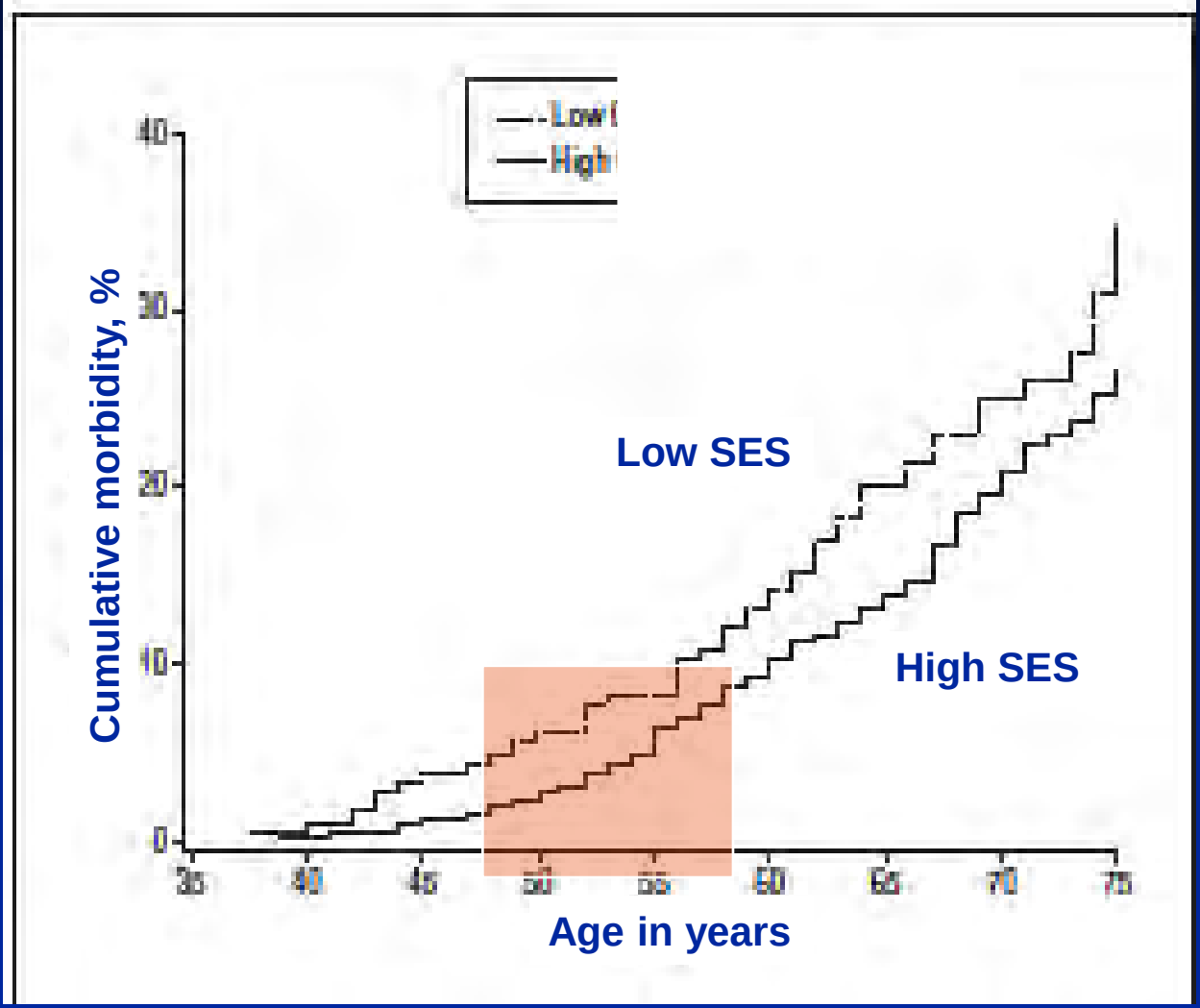


Caroline Bedell Thomas, MD 1904-1997

Johns Hopkins Medical School Class of 1951

Cumulative probability of coronary heart disease (MH, angina or other CHD): 1131 white, male Hopkins med students with annual follow-up

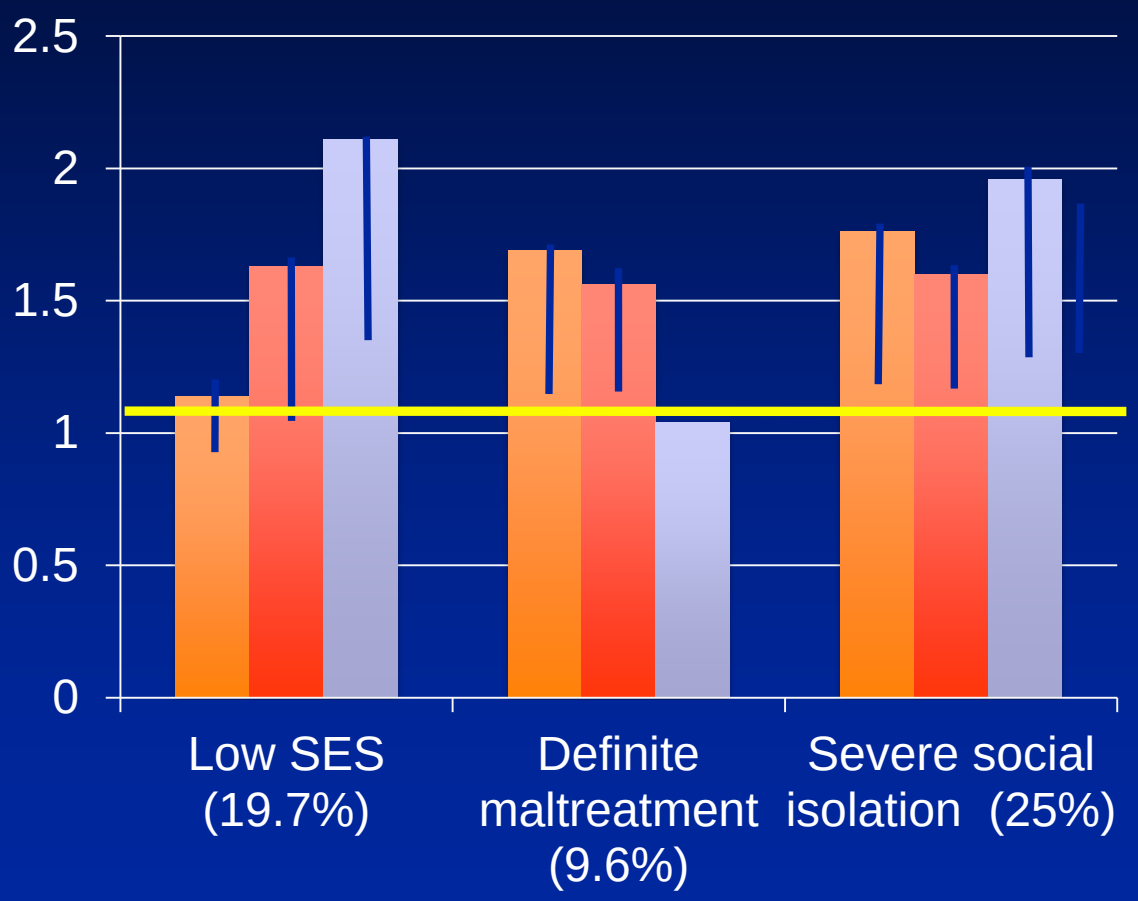
(The Johns Hopkins Precursor Study Caroline Thomas original PI JHMS Classes of 1948-1961



source MM Kittleson, 2006

Prospective study of childhood adversity before 11 and adult risk of illness at age 32: 972 in the Dunedin, NZ study

source A. Danese T Moffitt, 2009



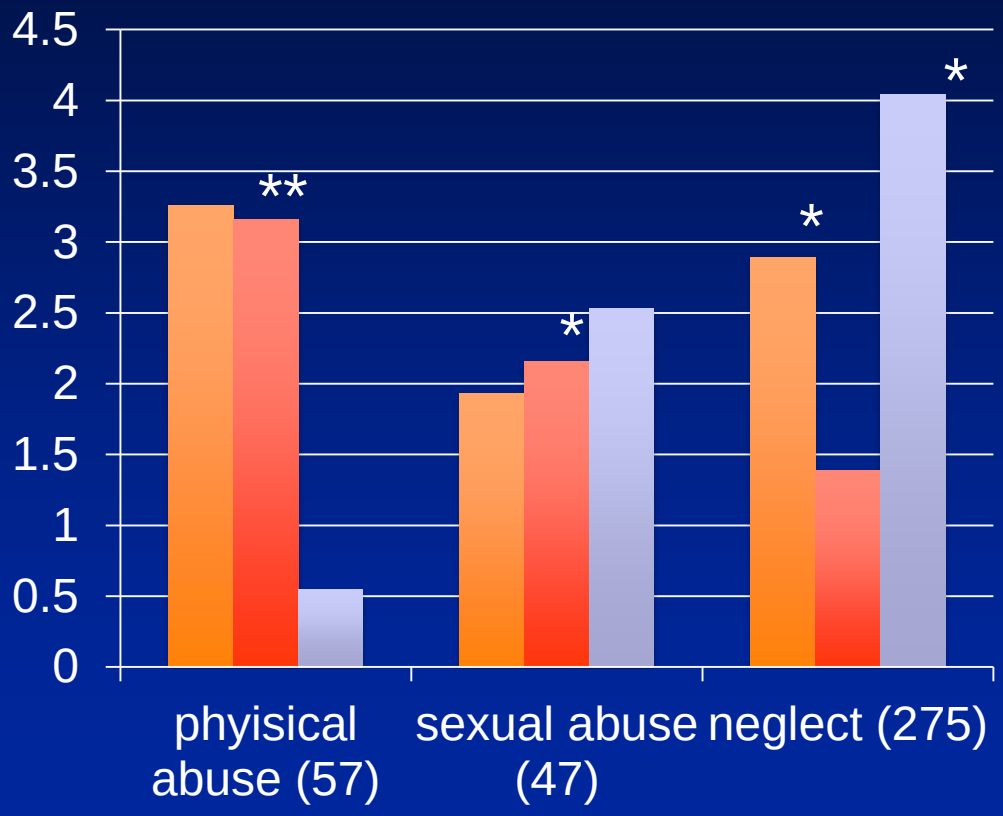
Controls:

- **Fam Hx cardiovasc**
- **and dep**
- **Birth wt**
- **Childhood BMI**
- **Current SES**
- **Current smoking**
- **Currenjt physical activity**
- **Current diet**
- **Current meds**

Note: At least 3 of 1) overwt; 2)hi BP; 3)hi cholest.; 4) lo high density LP; 5)hi HbA1c; 6) low 0^2 consumption

Documented child abuse and neglect before age 11 and objective signs of illness risk at age 40

source: C Widom 2012



HBa1c > 6%

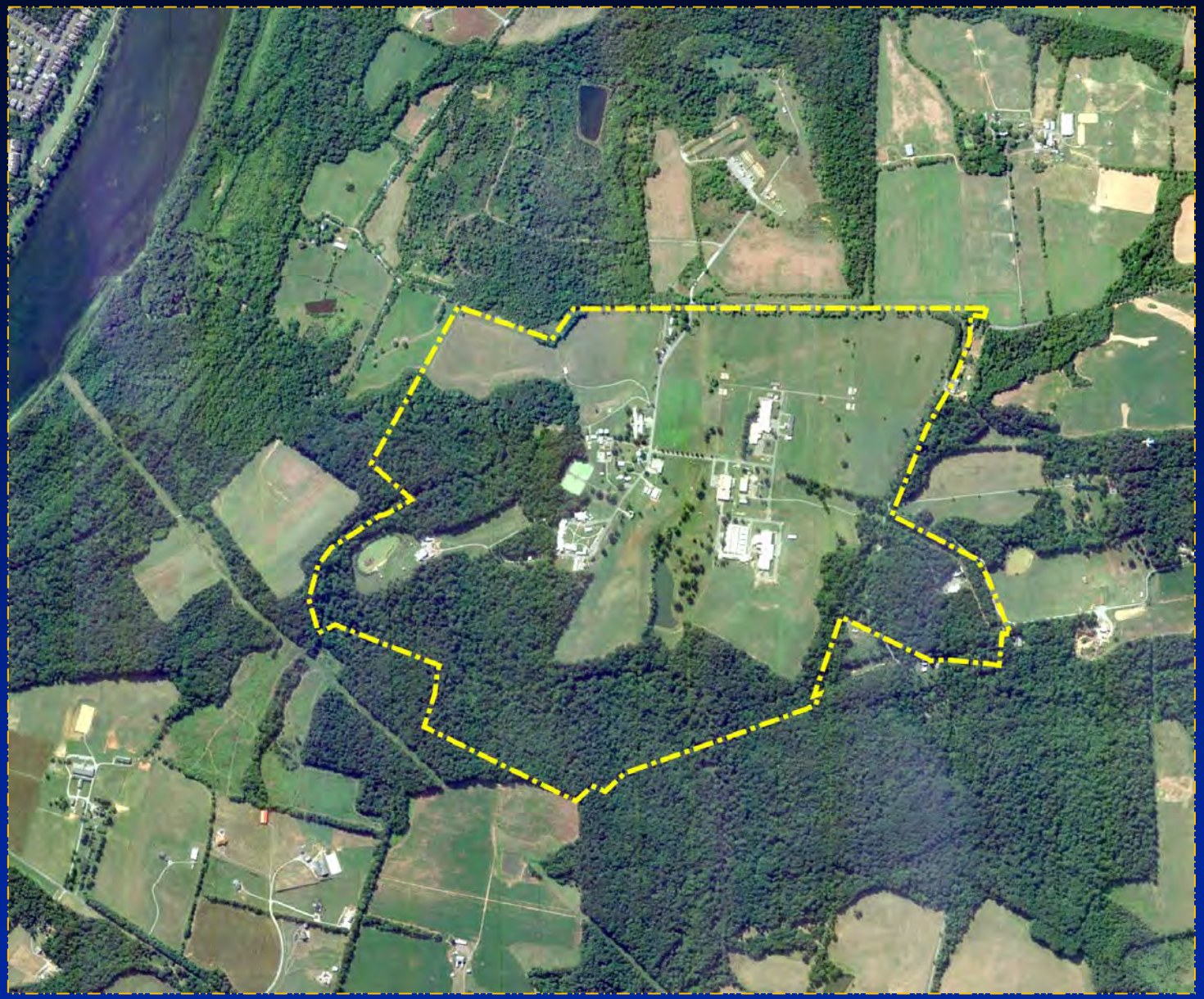
Malnutrition (BMI/lymphocyte/albumin)

Controls:

- **age**
- **gender**
- **race**
- **childhood SES**
- **adult SES**
- **smoking**
- **substance abuse**
- **depression/PTSD**

* $p < .05$ ** $p < .01$ in comparisons to 237 controls

Stephen Suomi



Experimental assignment to rearing conditions: health outcomes

source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

Mother rearing continued

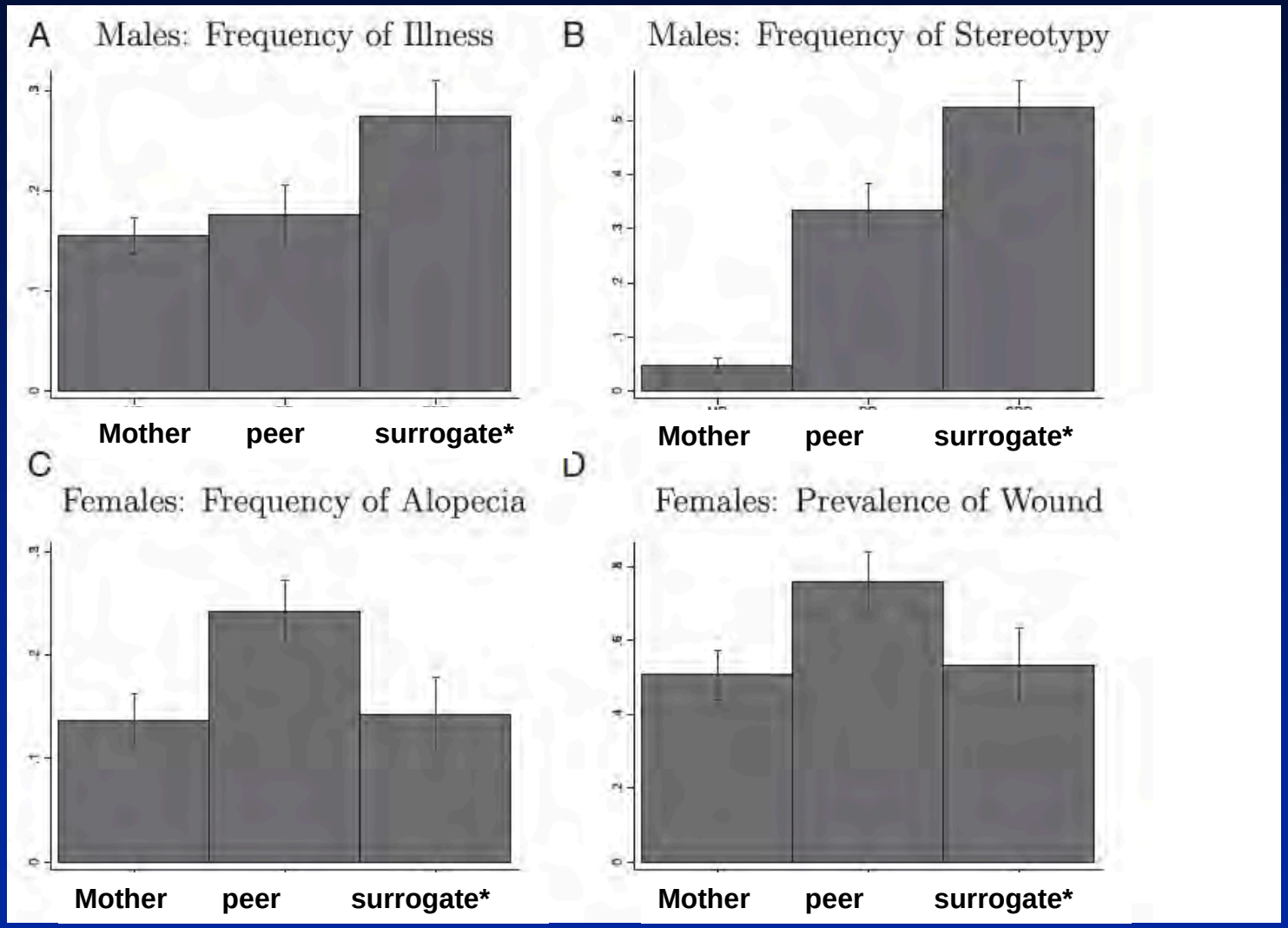
Nursery reared

Group housing

Observations of impaired medical and behavioral health

Timeline				
	Actual	37d	10-11 mos.	2 – 7 years
	Human equiv	4 mos.	3 years	6-21 years

Early childhood adversity and subsequent illness
source: Conti, G et al 2012



* Peer exposure 2 hr/d in first year

Elissa Epel

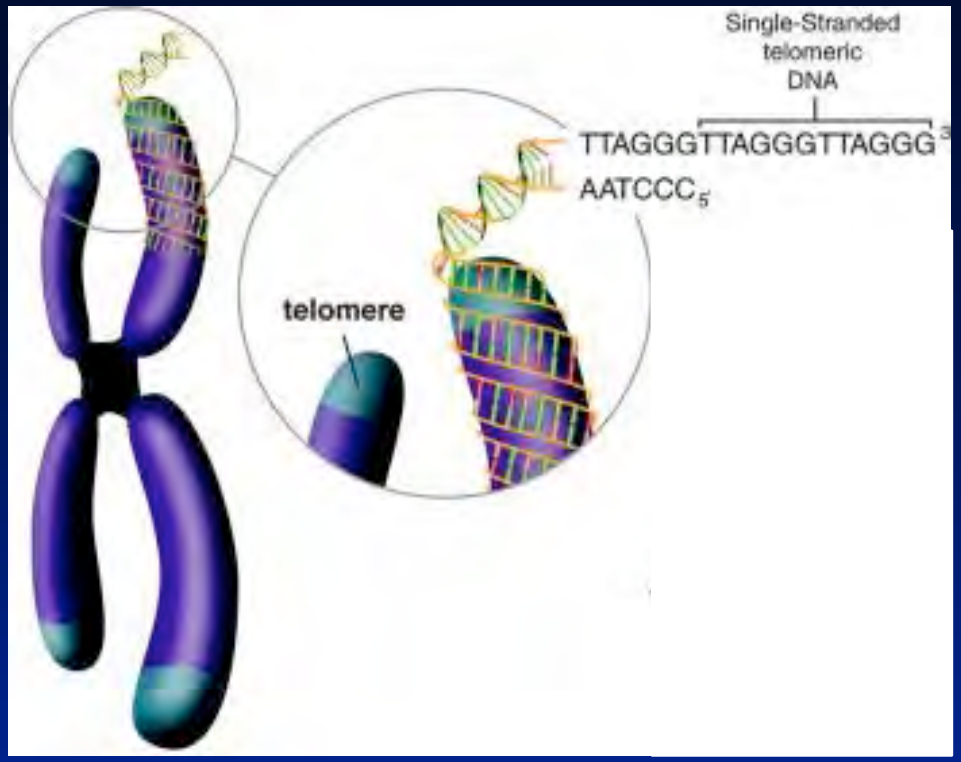
17312–17315 | PNAS | December 7, 2004 | vol. 101 | no. 49

Accelerated telomere shortening in response to life stress

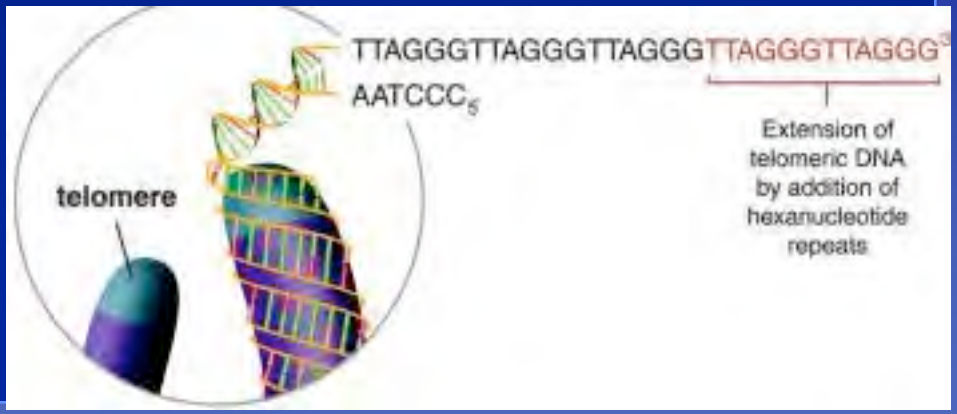
Elissa S. Epel*†, Elizabeth H. Blackburn‡, Jue Lin‡, Firdaus S. Dhabhar§, Nancy E. Adler*, Jason D. Morrow¶, and Richard M. Cawthon||

*Department of Psychiatry, University of California, 3333 California Street, Suite 465, San Francisco, CA 94143; ‡Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143; §Department of Oral Biology, College of Dentistry, and Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, Ohio State University, Columbus, OH 43210; ¶Department of Medicine and Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232; and ||Department of Human Genetics, University of Utah, 15 North 2030 E Street, Room 2100, Salt Lake City, UT 84112

Contributed by Elizabeth H. Blackburn, September 28, 2004

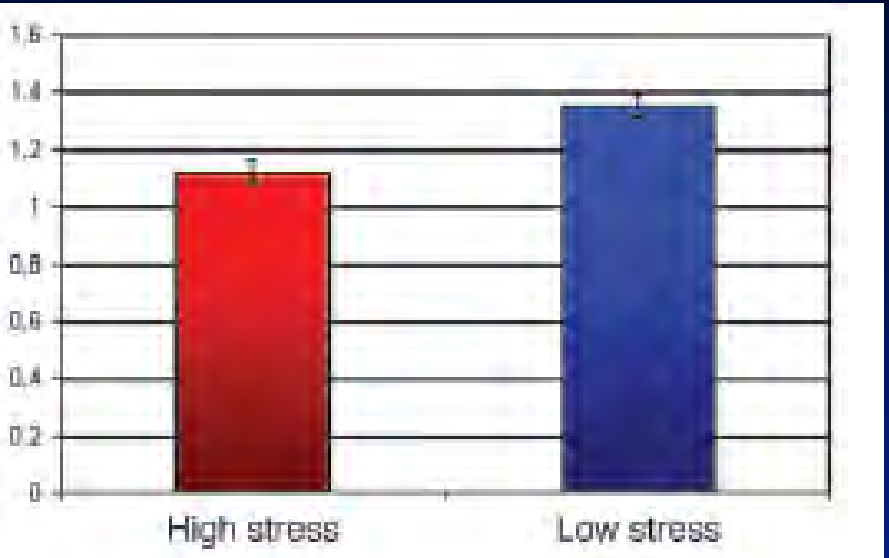

Single-Stranded
telomeric
DNA
TTAGGGTTAGGGTTAGGG
AATCCC5
telomere

Telomerase

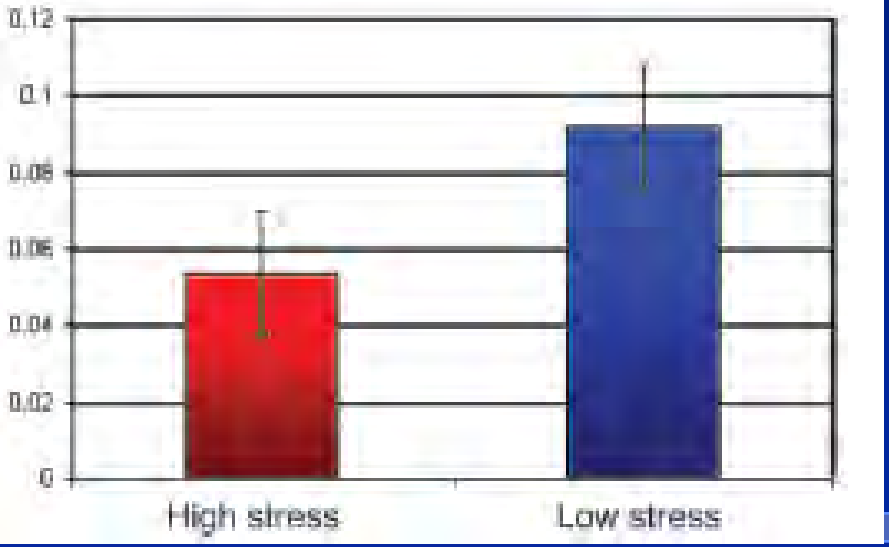

TTAGGGTTAGGGTTAGGGTTAGGGTTAGGG
AATCCC5
telomere
Extension of
telomeric DNA
by addition of
hexanucleotide
repeats

39 care giving mothers **19 mothers of healthy children**

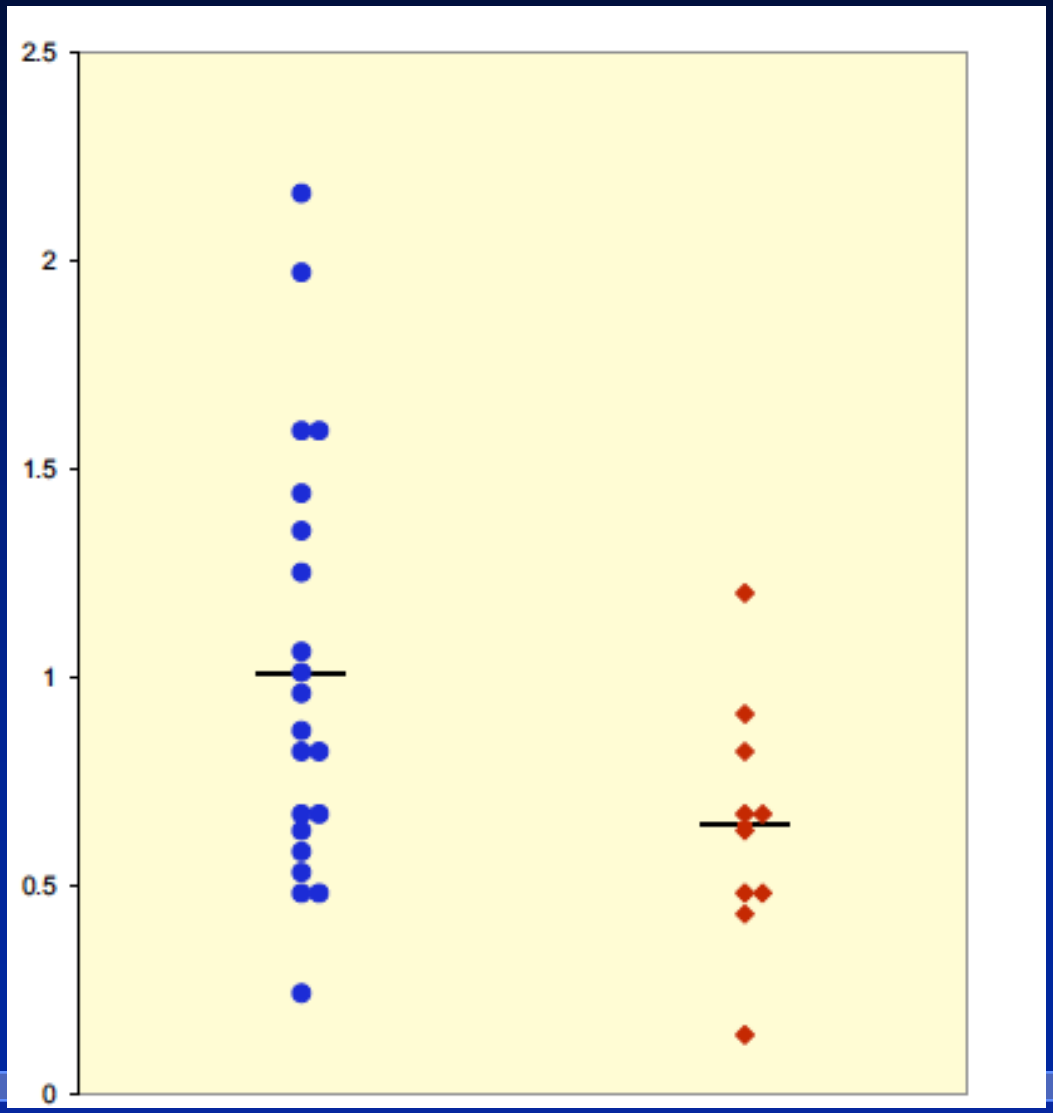
Telomere length



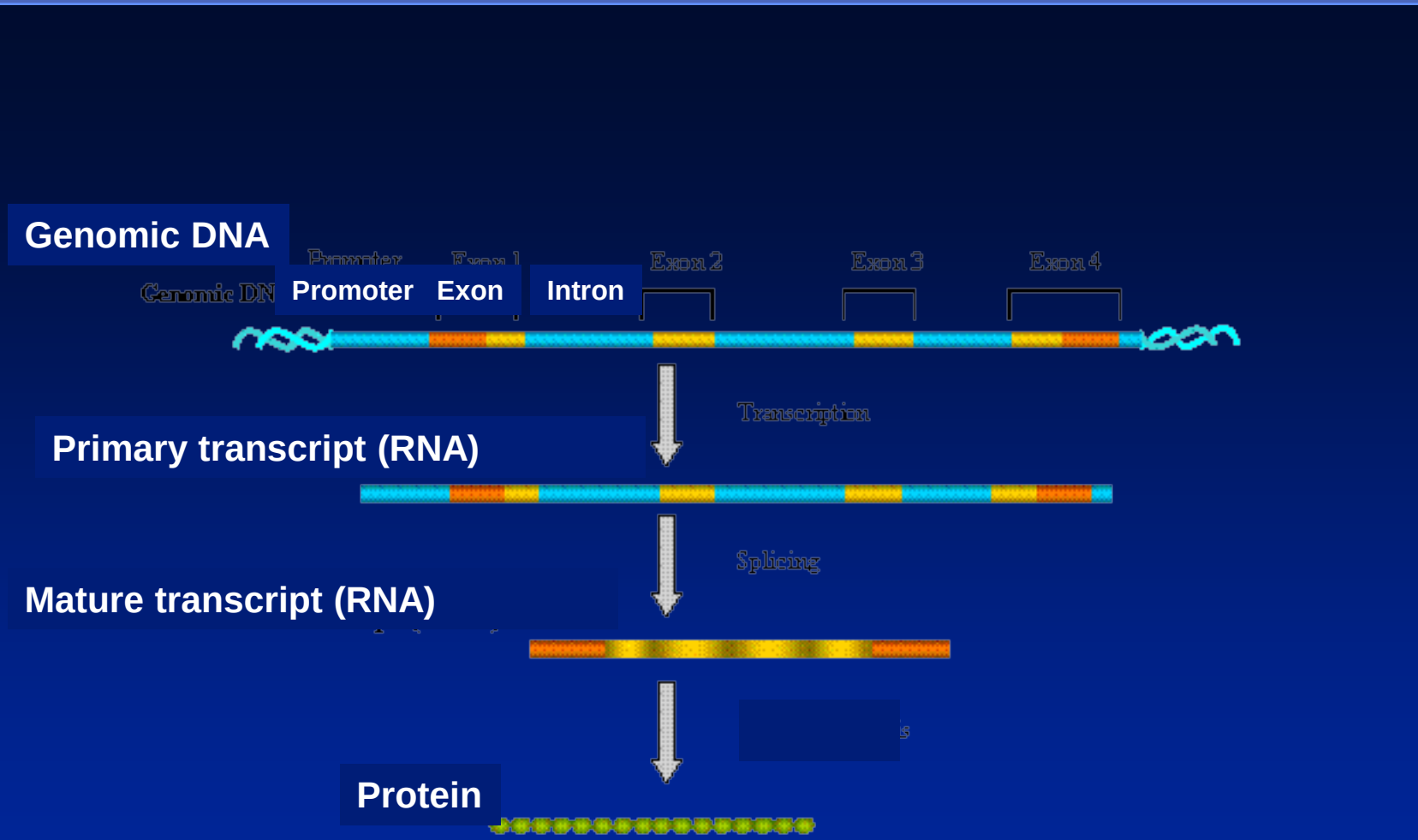
Telomerase levels



Telomere length and adult reports of maltreatment “when I was growing up.”



Source:
A Tryka, 2010


Genomic DNA
Promoter
Exon
Intron
Exon 2
Exon 3
Exon 4
Transcription
Primary transcript (RNA)
Splicing
Mature transcript (RNA)
Protein

Experimental assignment to rearing conditions: health outcomes

source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

Mother rearing continued

Nursery reared

Group housing

Observations of impaired medical and behavioral health

Timeline				
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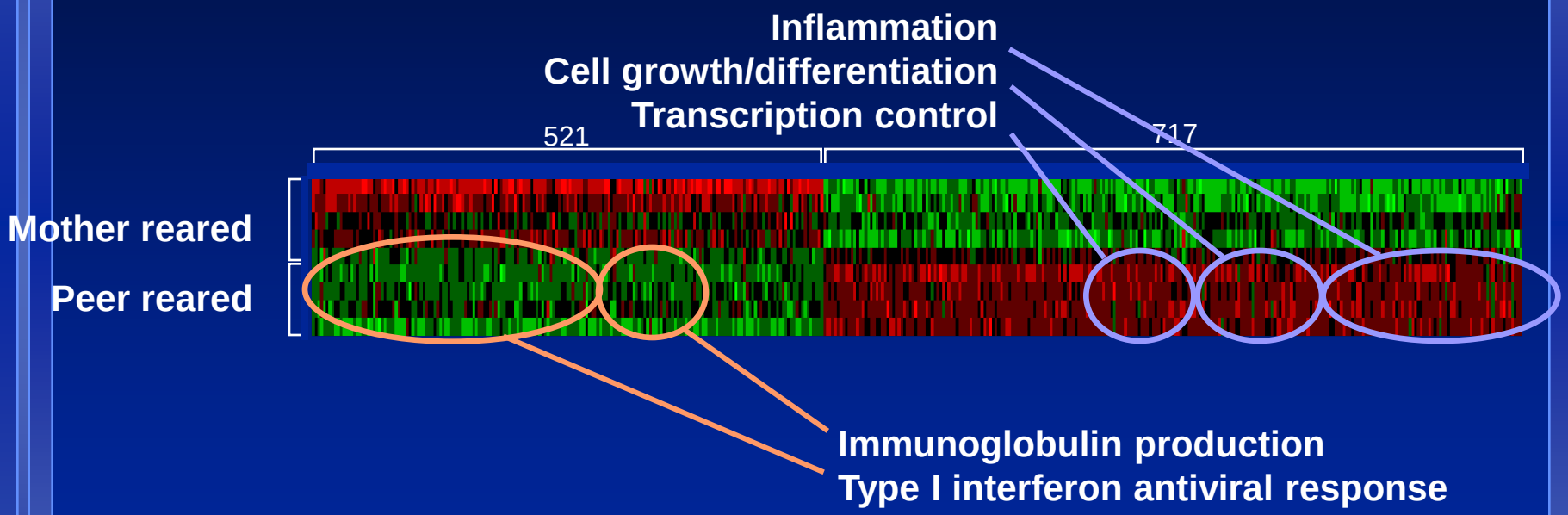
Suomi

Down regulated

Early life social conditions

S

Up regulated



Adolescent Twin Study

Robert Plomin, IOP (UK)
Mavis Hetherington, UVa
Jenae Neiderhiser, Penn State
Jody Ganiban, GWU

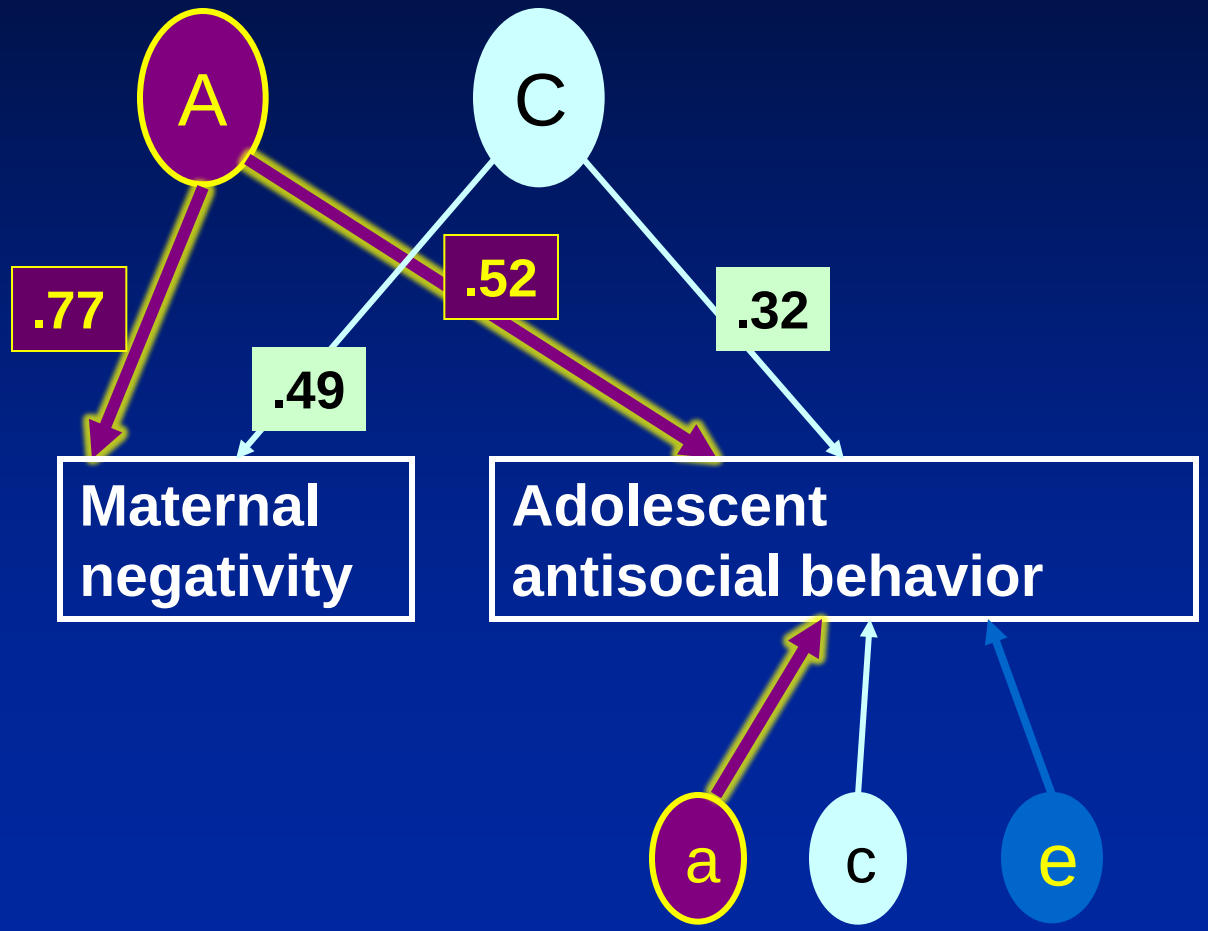
Adoption Study

Leslie Leve, U Oregon
Jenae Neiderhiser, Penn State
Danny Shaw, Pitt
Jody Ganiban, GWU
Pasco Fearon UCL (UK)

NIH/NIA Project on early adversity (“Reversibility”)

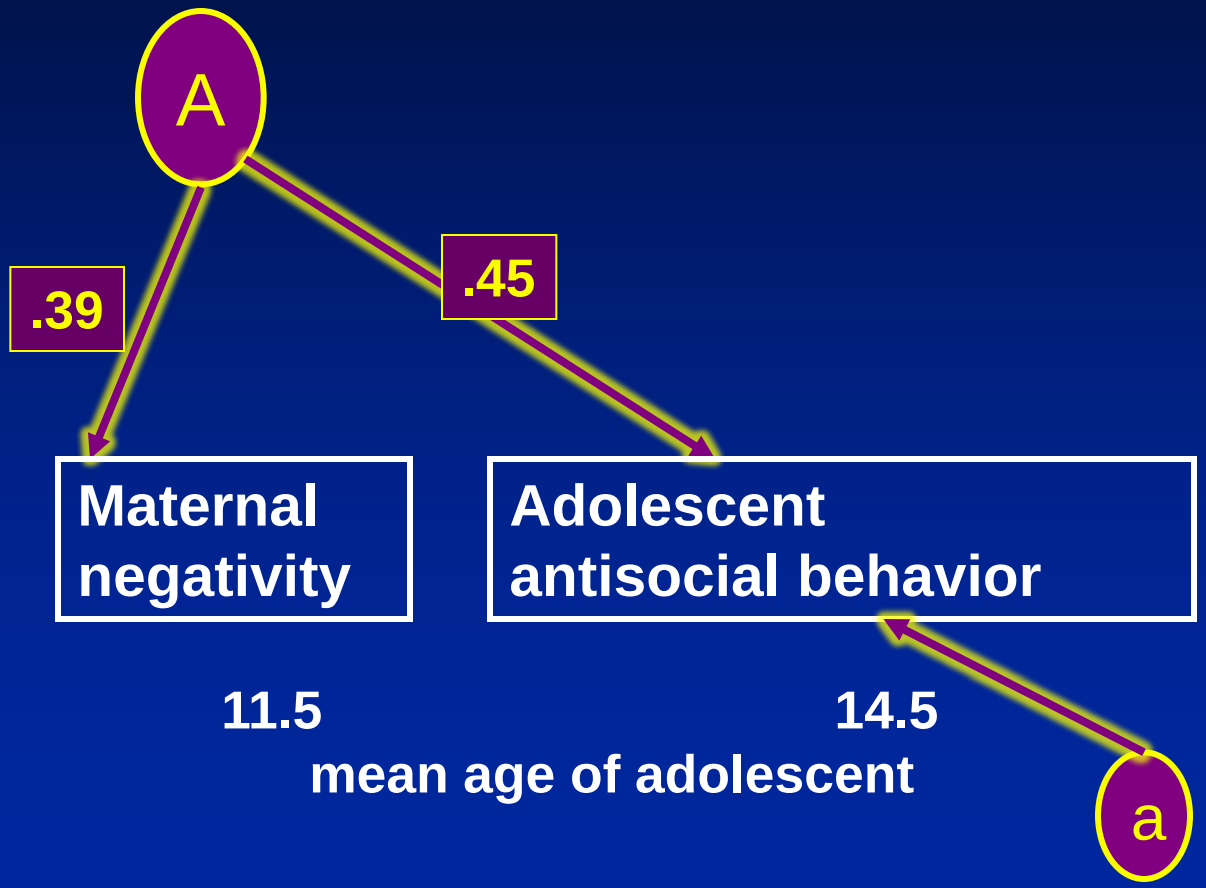
Stephen Suomi, NICHD
Richard Suzman, NIA/BSR
Lisbeth Nielsen, NIA/BSR

Maternal negative and and adolescent antisocial behavior: contemporaneous analysis at age 12.5



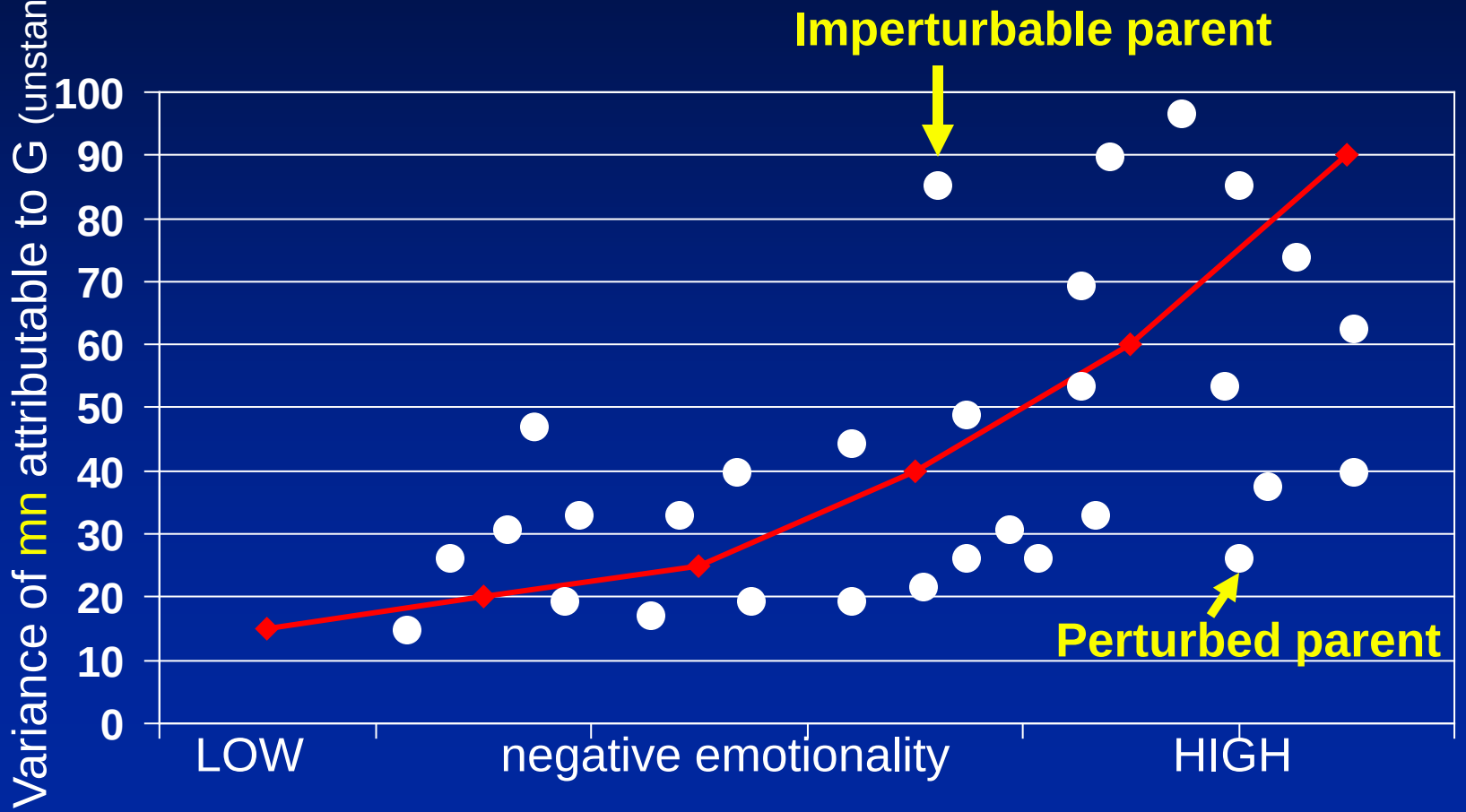
Common genetic influence on association between prior parenting and subsequent antisocial behavior

(controlling for stability, contemporaneous associations and adolescent asb -> maternal negativity)



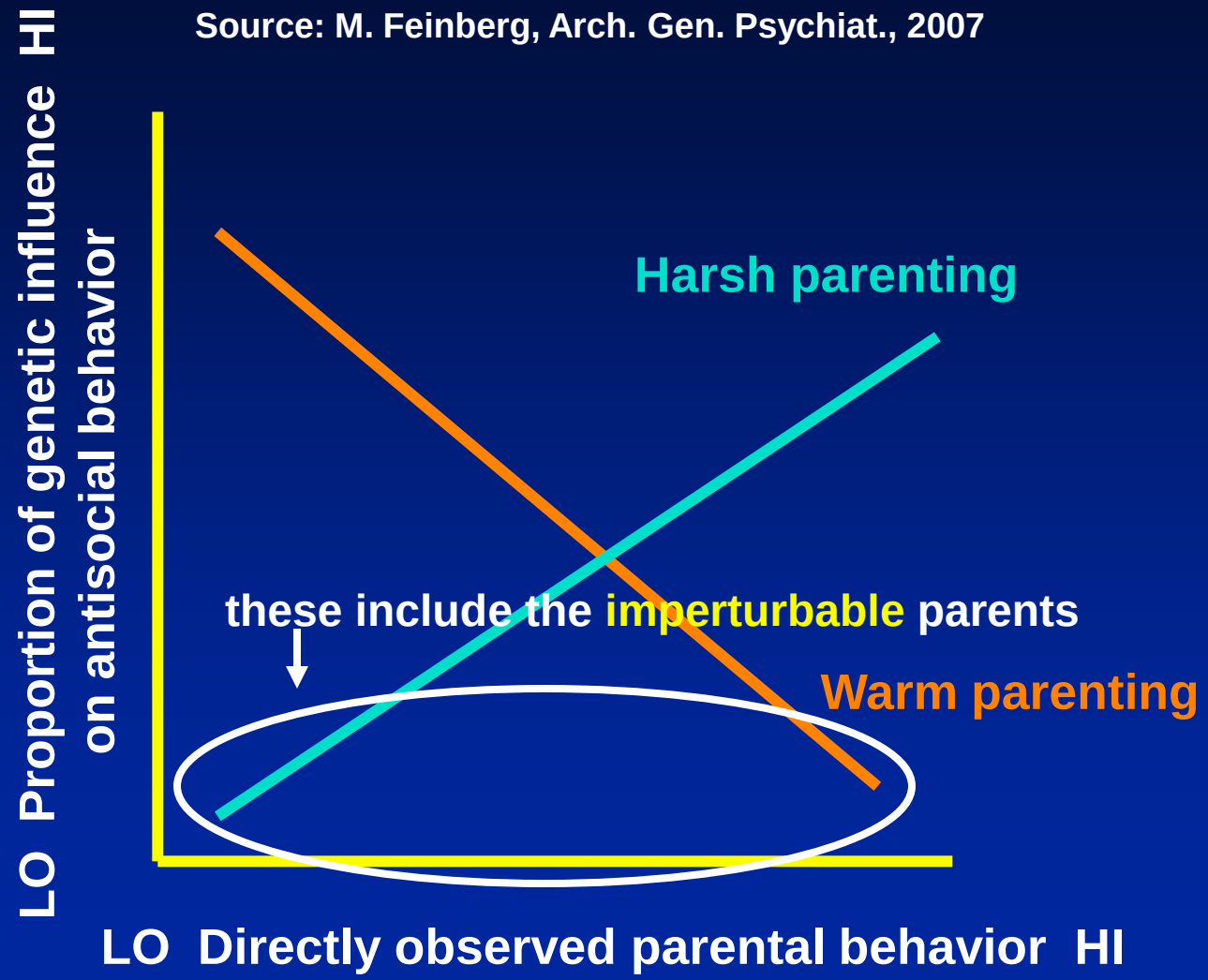
The relationship between child temperament and maternal negativity and conflict

Source: J Ganiban, 2011



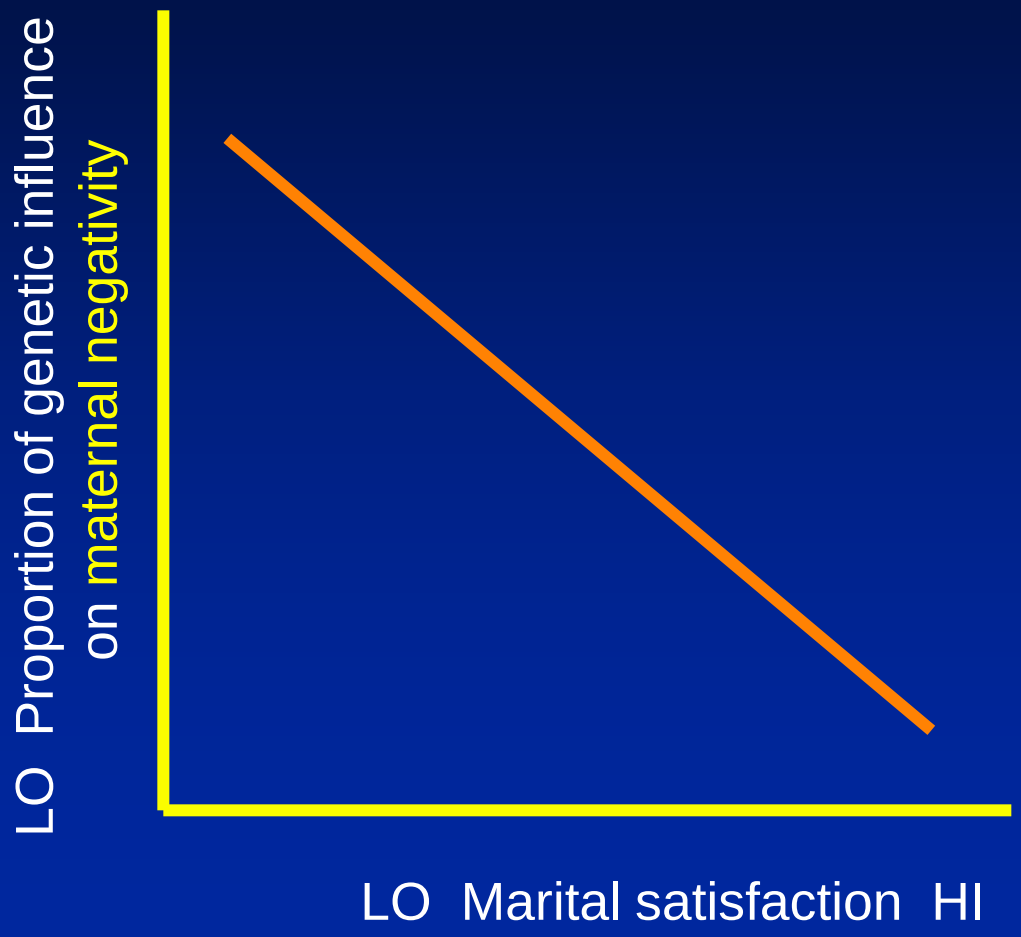
Parental behavior and expression of genetic influence on antisocial behavior

Source: M. Feinberg, Arch. Gen. Psychiat., 2007



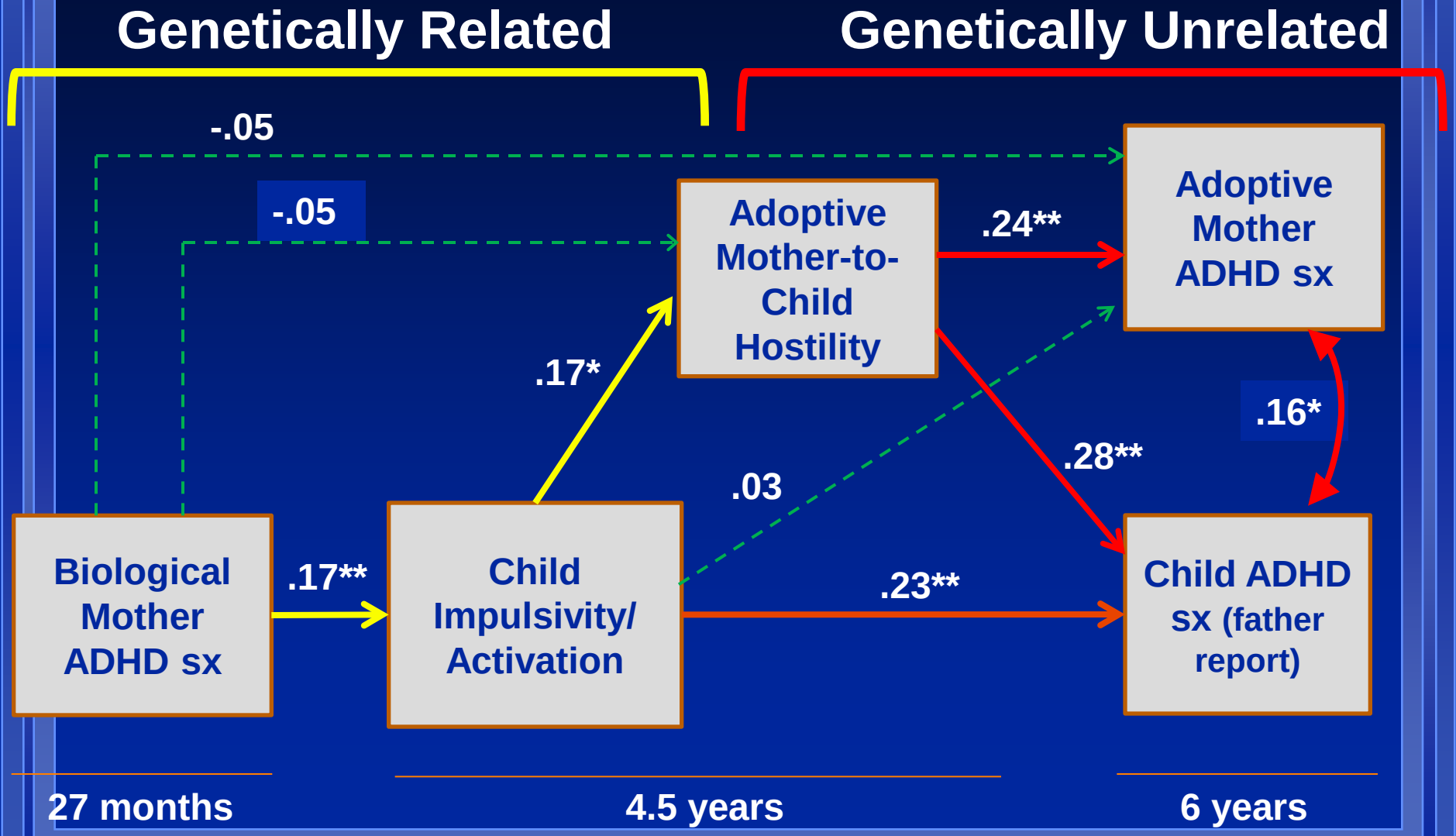
Parental behavior and expression of genetic influence on disinhibited behavior

Source: J. Ulbricht, 2013

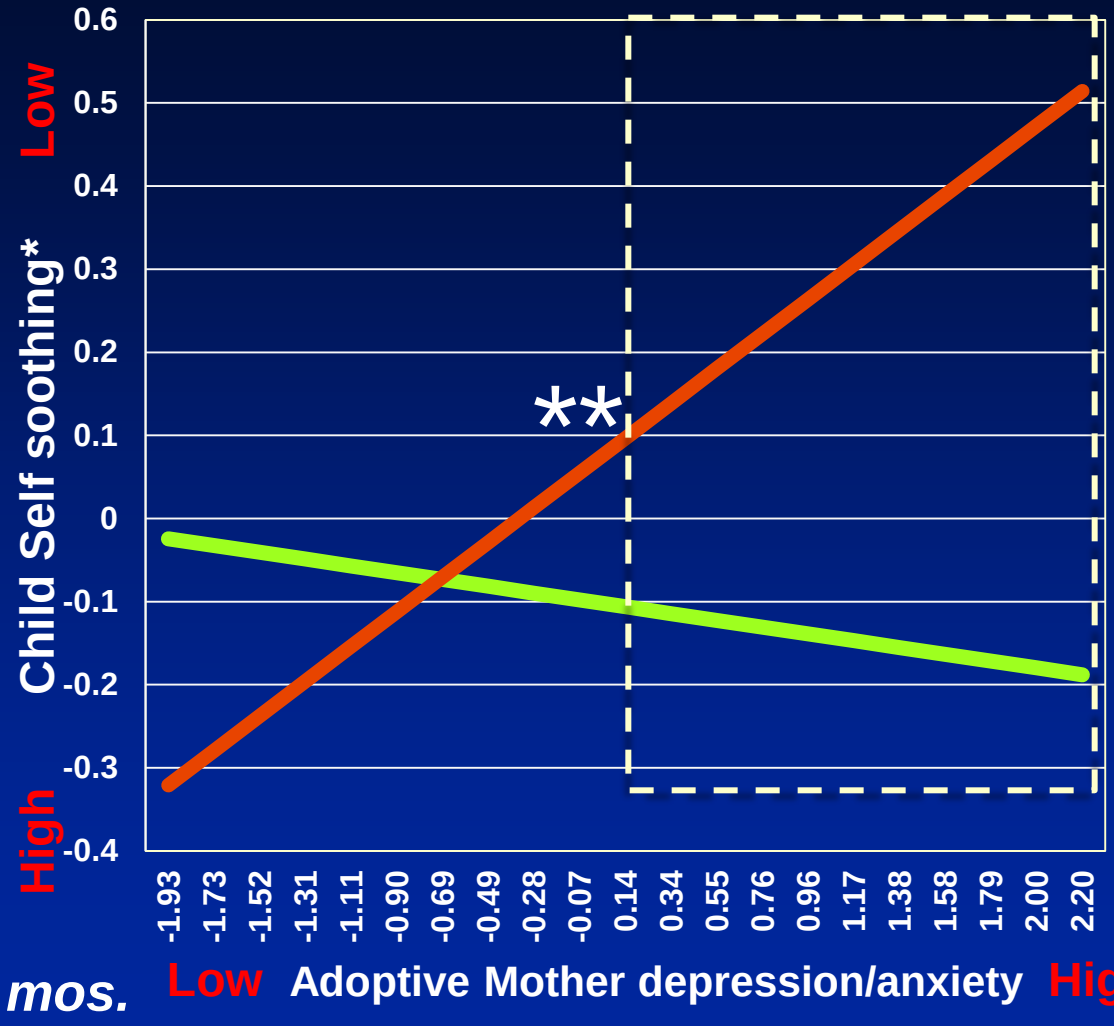


Evocative *r*GE on Child ADHD Symptoms

(G .Harold et al., JCPP in press)



Child's genetic risk for SUDs and mother's depression/anxiety n = 361



BM high externalizing

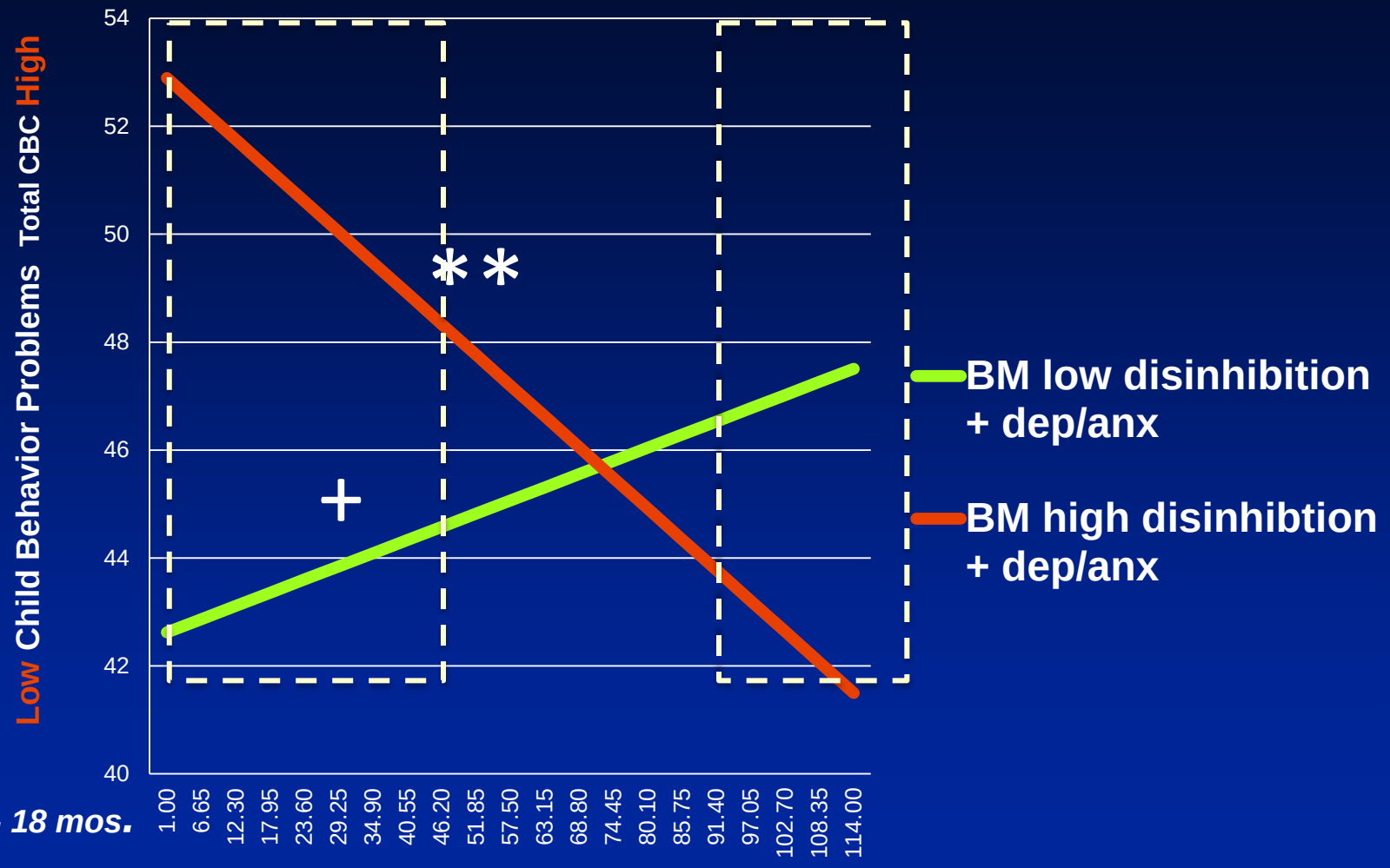
BM low externalizing

*Attention frustration task

Source L. Leve, Child Develop. '10

Children at low and hi risk for SUD (+) & adopted mothers structured parenting

(n = 361)

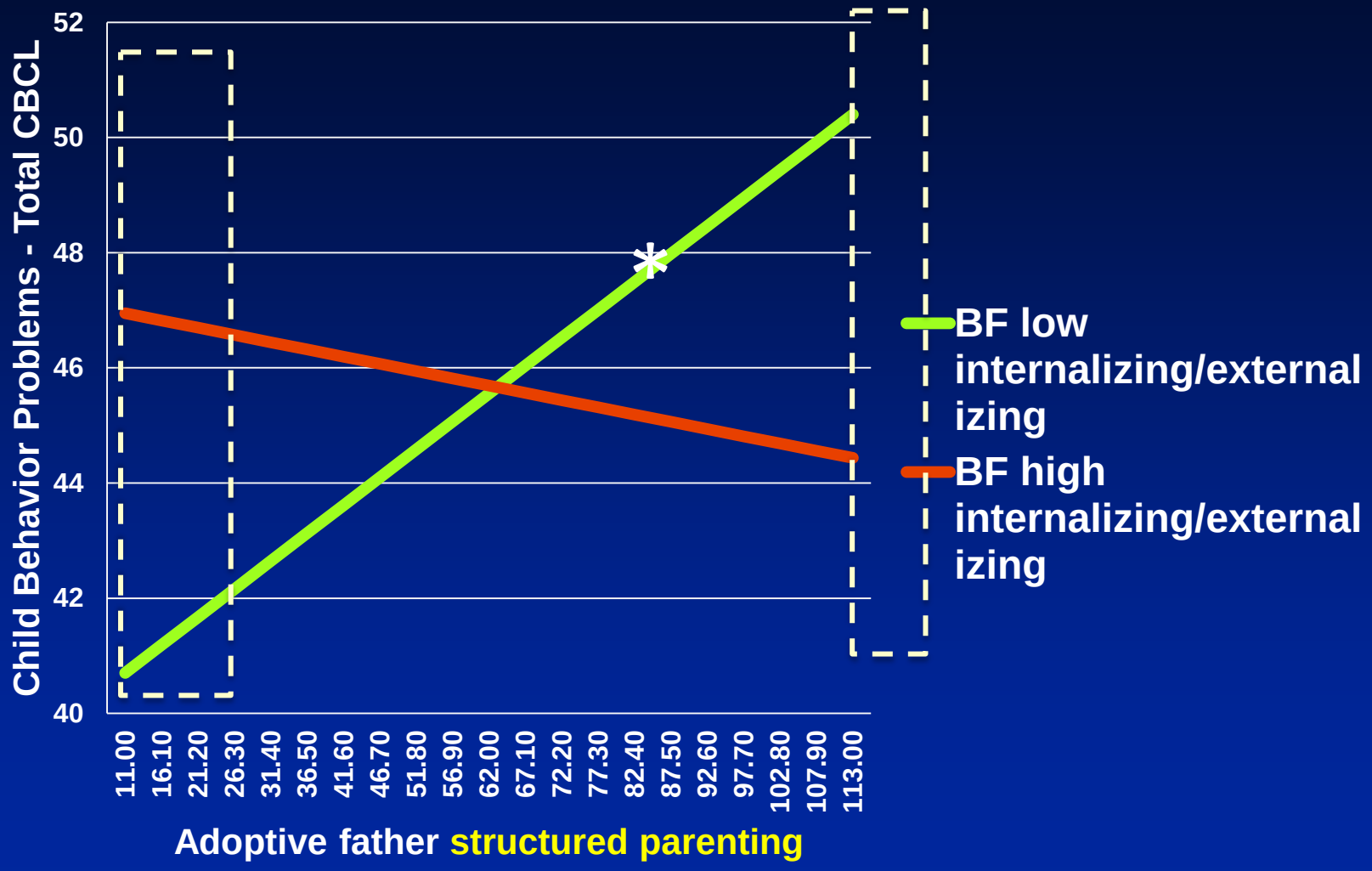


* Coded videotape

Source: L Leve, JAACAP, 2009

Children at low and hi risk for SUD (+) & adopted fathers structured parenting

(n = 95)



Source: L Leve, JAACAP, 2009

Photo Source: drugfree.org

Photo Source: Strategies for Success (Chandler, AZ), 2012

Photo Source: child abuse weekly